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SOLUTE MIGRATION DURING DRYING OF DAMP POWDER BEDS

by

© NAWAR SELIM AL-NUAIMI

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH

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OF MASTER OF SCIENCE

IN

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FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled "Solute Migration During Drying of Damp Powder Beds" submitted by Nawar Selim Al-Nuaimi in partial fulfilment for the requirements for the degree of Master of Science in Pharmaceutics.

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ABSTRACT

Studies were undertaken to investigate the migration of the water soluble dye amaranth in damp powder beds during drying under controlled conditions. Beds of water-soluble and water-insoluble powders were used, wetted with purified water. Lactose B.P. and calcium sulfate dihydrate proved to be suitable for this type of study.

A procedure was developed for the quantitative determination of amaranth at different depths in the bed by using a lathe milling machine, and spectrophotometer. Drying conditions under which the study was conducted were established first. Measurements of the temperature distribution, drying rate and moisture distribution were made under the same conditions. The measurements of temperature and moisture distribution in the powder bed helped in understanding what was occurring in the body during the drying process.

The drying mechanism was visualized as consisting of three zones: constant rate period, first falling rate period and second falling rate period. There was no clear distinction between the first and second falling rate periods. The temperature gradient in the bed resulted in diffusion of vapor within the bed along the vapor pressure gradient. In both systems amaranth migrated to a large extent in the early stages of the drying process.

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INTRODUCTION

An appreciable amount of work has been reported on the drying process (1-20). In these previous studies attention was drawn to the influence of liquid movement on the rate of drying of stationary beds of saturated porous materials with one exposed surface. It was shown that the changes in the rate of drying with average moisture content, and the moisture gradient in the bed at various stages of drying, provide information from which the direction and extent of liquid movement may be predicted. Generally there are two stages in the drying process. In the first stage the liquid moves to the exposed surface of the bed and evaporates. In the second stage the liquid evaporates in situ within the bed and the vapor diffuses to the exposed face. If the liquid contains a solid in solution the solid will be deposited during drying in the zones where evaporation takes place. It follows, therefore, that although initially the solute may be uniformly distributed throughout the moist bed it will tend to be segregated through liquid movement as the bed progressively dries.

Many examples of this phenomenon occur in practice and some have important consequences. For example, the preparation of pharmaceutical tablets in large quantities using a rotary tableting machine depends on obtaining the material to be compressed in a free-flowing form which will run easily from the feed hopper into the die. The usual method for preparing the feed-stock is to wet-granulate the

powder and then to dry the granules. Although this method is intended to produce granules of uniform composition, it has been established that under certain drying conditions the outer layer of the granule will have a composition different from that of the core. Thus a tablet produced from granules in which the binder is concentrated in the outside layer of the granules is liable to have localized areas of high cohesion, which resist subsequent disintegration and dissolution (26).

Compressed tablets are probably the most widely used dosage form for the administration of orally effective therapeutic agents. It follows then that migration of the potent ingredient in some tablets, especially in the case of a solvent-soluble, low dosage drug, is of great importance. To this end, specifications have been established to control content uniformity of such tablets (U.S.P., B.P.).

REVIEW OF THE LITERATURE

Drying procedures, like other important unit operations in pharmacy such as particle size reduction and blending of solids, have received relatively little attention in the pharmaceutical literature. Within recent years, however, a growing interest in these pharmaceutical engineering areas has become apparent.

1. Theory of Drying

Drying involves both heat and mass transfer operations. Heat must be transferred to the material to be dried in order to supply the latent heat required for vaporization of the moisture. Mass transfer is involved in the diffusion of water through the material to the evaporating surface, the subsequent evaporation of the water from the surface, and diffusion of the resultant vapor into the passing air stream.

The drying process can be more easily understood if attention is focussed on the film of liquid at the surface of the material being dried. The rate of evaporation of this film is related to the rate of heat transfer by the equation (1)

$$dw/d\theta = q/\lambda$$

where $dw/d\theta$ is the rate of evaporation in pounds of water per hour; q is the overall rate of heat transfer to the drying surface (Btu per hour); and λ is the latent heat of vaporization of water (Btu per pound).

The rate of diffusion of moisture into the air

stream is expressed by rate equations similar to those for heat transfer (1).

The rate equation is

$$dw/d\theta = K'A(Hs-Hg)$$

where $dw/d\theta$ is the rate of diffusion expressed as pounds of water per hour, K' is the coefficient of mass transfer [pounds of water/(hour) (square foot) (absolute humidity difference)], A is the area of the evaporating surface in square feet, Hs is the absolute humidity at the evaporating surface (pounds of water per pound of dry air), and Hg is the absolute humidity in the passing air stream (pounds of water per pound of dry air).

After an initial period of adjustment, the rate of evaporation is equal to the rate of diffusion of vapor, and the rate of heat transfer can be related to the rate of mass transfer:

$$dw/d\theta = q/\lambda = K'A(Hs-Hg)$$

If the overall rate of heat transfer, q, is expressed as the sum of the rates of heat transfer by convection, radiation and conduction, the above equation may be expanded to the form

$$dw/d\theta = (qc + qr + qk)/\lambda$$
$$= K'A(Hs-Hg)$$

where qc, qr and qk are the rates of heat transfer by convection, radiation and conduction, respectively.

The above equation holds as long as there is a film of

moisture on the surface of the material being dried. When the surface becomes partially or completely dry, the heat and mass transfer equations become more complex. In this case, the rate of drying is controlled by the rate of diffusion of moisture from the interior of the material, as well as the rate of heat conduction to the evaporation zone. This diffusion is greatly influenced by the molecular and capillary structure of the solid. The process becomes further complicated when the drying surface causes a shrinkage of the solid. This phenomenon can cause blocking and distortion of the capillary structure and thus interfere with the transfer of internal water to the surface of the material. An example of this is the so-called "case hardening" phenomenon in which the surface of the solid becomes harder than the interior and less permeable to the transmission of interior moisture (1).

2. Drying Rate

One of the earliest works on drying was reported in 1921 by Lewis (2). He postulated that the drying of a solid involved a balance between the evaporation of the moisture from the solid surface and the rate of movement of the moisture from within the solid to the drying surface.

Sherwood (3) developed a theory (with experimental confirmation) showing three possible distinct stages in the drying process. These stages were described as:

a) a constant rate period;

b) a falling rate period during which there was a reduction in the size of the wetted surface with a proportional reduction in the drying rate;

c) a second falling rate period during which the liquid evaporated from the surface as fast as it could get there by diffusion from the interior of the solid.

It was not until some years later that consideration was given to diffusion of vapor from the interior of the solid (5).

Fisher (4) showed that the drying of a surface-dried particulate material exhibited a number of distinct drying periods. The material dried at a constant rate until a "critical point" was reached (this point marked the instant when the liquid water on the surface was insufficient to maintain a continuous film covering the entire drying area). The period subsequent to the critical point was called the falling rate period. In the first part of this period the decrease in the drying rate was linear, while in the second period the drying rate was non-linear and was usually an asymptotic, exponential approach to equilibrium moisture content with respect to time.

Gilliland (5) considered the drying of slabs of different materials in which the initial concentration of water was uniform and sufficiently high so that the surface was completely covered by a water film. He found that the

drying rate during the constant rate period depended only on the external conditions. He also pointed out that during the constant rate period, the rate of evaporation from various materials under comparable conditions should be the same. The constant rate period was terminated when the surface dried to a point where it could not maintain a saturated air film above the bed. At this point the first falling rate period began and continued until the surface of the bed was completely dry. During the second falling rate period, which followed immediately, it was claimed that vaporization occurred within the bed, with vapor in turn diffusing to the surface.

Bartlett (6) carried out very precise measurements of drying rate. He found that the constant rate period was not truly constant, and that the break between the constant and falling rate period was not as sharp as was often indicated in the literature. He showed that during the early part of the drying process the drying rate decreased gradually. At the critical moisture content the drying rate was usually about five percent less than its value at saturation of surface. In the falling rate period there was a more rapid, but smooth, decrease in the drying rate. This behavior emphasized that the drying process was a unified continuous process even though there might be a change in the importance of the various mechanisms which transport heat and mass.

Adams (7) later studied the drying of Penton[a], porous carbon blocks and polystyrene spheres. He concluded from his experiments that the transition from the constant rate period to the falling rate period was not a result of any drastic change in the drying process mechanism. It resulted instead from a continual decrease in wetted surface area and a slight increase in the thickness of the surface layer of vaporization, accompanied by an increase in the surface temperature in those cases that were initially below the wet-bulb temperature. Adams was of the opinion that the importance of the critical moisture content was exaggerated by investigators. He suggested that there was a gradual change in the drying rate from the constant rate period to the falling rate period. Adams studied the temperature distribution in beds of polystyrene spheres and reported that the psuedo-wet-bulb temperature, as defined by Nissan et al. (18), was established only when the lower surface of the bed was nearly adiabatic and then only after the surface of the bed became dry.

3. Drying Mechanism

Sherwood (8) in his study of the drying process, proposed a liquid diffusion mechanism for the transfer of liquid from within the solid to its surface. He described this mechanism by an equation analogous to the Fourier heat

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[a] Chlorinated polyether; Hercules Powder Company, Wilmington, Delaware, U.S.A.

conduction equation. A further contribution was made by Newman (9, 10) who presented solutions to Sherwood's liquid diffusion equation for a number of geometrical shapes. Later it was pointed out by Sherwood and Comings (11) that the mechanism of moisture movement through the solid apparently was not one of liquid diffusion. Instead, the liquid was thought to move to the surface of the material under the influence of capillary forces. They also found that Newman's model did predict the drying curve for some materials with fair accuracy. Ceaglske and Hougen (12) demonstrated that the diffusion equations developed by Sherwood and Newman did predict the drying rate of a large number of materials such as soap, clay, sand and wood. Their moisture distributions were determined by sectioning the sample after a fixed drying time and then weighing each section before and after removing all of the water in a drying oven. They were also able to confirm that in many materials liquid moved to the surface by capillary action rather than by diffusion.

Pearse, Oliver and Newitt (13) explained the mechanism of drying on the basis of the shape of the drying rate curve. Figure 1 represents typical drying rate curves adapted from Sherwood (14) in beds of granular solids composed of non-porous particles. It has been shown that granular solids in which capillary forces are responsible for movement show drying rate curves similar to Curve A.

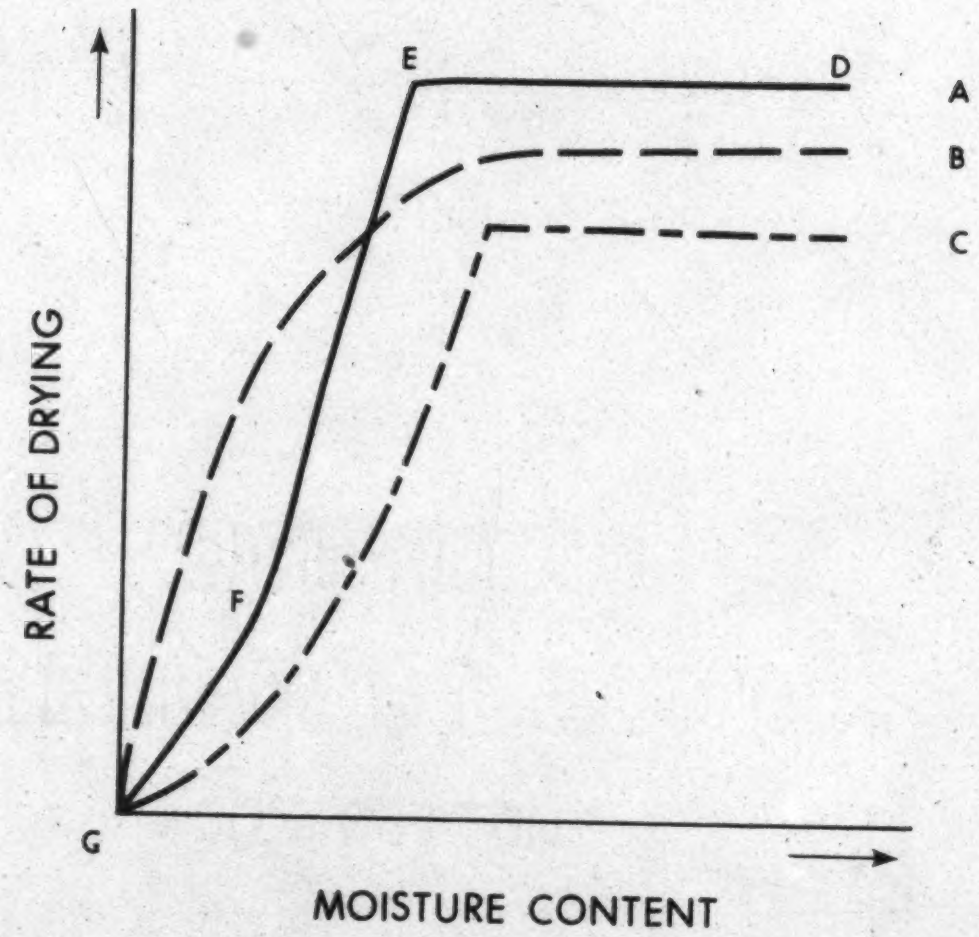

Figure 1

Typical Drying Rate Curves
in Beds of Granular Solids
[Adapted from Sherwood (14)]

In such a curve there are three fairly well defined segments: DE, EF and FG. These segments are usually distinguished as the constant rate period, the first falling rate period, and the second falling rate period, respectively. The transition points become less clearly marked as the particle size decreases.

As stated by Pearse et al., solids in which moisture movement was mainly by vapor diffusion should exhibit drying rates corresponding with curves B or C. Solids in which the moisture movement was accomplished either by capillary action only or modified by vaporization, should have drying rate curves similar to curve A or B, according to the conditions under which drying took place.

Pearse et al. studied the forces affecting the movement of liquid in a porous bed. These forces were reported to be gravity, friction, convection and capillarity. The authors used beds of spherical particles in random packing, taking into consideration resistance to flow and suction potentials[a], in order to determine the importance of these forces with particles having radii from 10^{-1} to 10^{-6} cm. The results showed that for systems composed of particles in the 10^{-1} to 10^{-2} cm range gravitational and capillary forces controlled water movement. For beds containing particles in the 10^{-2} to 10^{-4} cm range capillary force alone

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[a] Westman (15) defined the suction potential as the pressure necessary to force gas into the moist solid and expel the water from the capillaries.

was responsible, while for beds composed of 10^{-5} to 10^{-6} cm particles, capillary and frictional forces controlled the water movement.

Oliver and Newitt (16) continued the work with the measurement of suction potentials. They were interested in the drying of granular solids with particle sizes 2.5×10^{-4} cm to 6.0×10^{-4} cm radius. Their data indicated that in the case of granular solids composed of non-porous particles, moisture movement was governed by the structure of the bed. Two categories could be distinguished: beds where capillary forces controlled the movement of moisture, and beds where the capillary forces were limited by vaporization within the pores. The authors claimed that there was no sharp distinction between these two categories. Subsequently a third category was defined, in which the structure of the bed was such that, under one set of conditions, capillary force was the controlling factor, while under another set of conditions, the vaporization exerted the major influence in the movement of moisture.

Corben and Newitt (17) studied the mechanisms of moisture movement in porous granular beds. They considered a bed with both the internal pores and the external voids initially saturated with water. They reported that as drying commences and the surface water retreats into the surface voids and pores, a suction potential will build up in the liquid within the bed and, after a relatively small

moisture loss, the entry suction potential of the largest surface voids would be reached. Air will enter, and the displaced water will be transferred to the smaller surface voids and pores. Successively finer voids will open as the suction potential progressively increases with further drying. The size of voids opening at any depth will be dependent upon the effective suction potential at that level as determined by the surface suction potential modified by gravitational and frictional forces.

The difference between drying rate curves of porous granular material and the corresponding beds of non-porous granular material was considered to be the capillary action of the internal pores of the porous granules in conveying water to the surface.

Corben and Newitt felt that this factor was sufficient to account for the higher rate of drying observed for the porous materials during the constant rate period. They showed that after the first falling rate period there was a very rapid reduction in the drying rate, followed by a prolonged second period in which the drying rate fell very slowly. Throughout the different stages of drying there were certain differences observed in the moisture distribution between porous and non-porous materials. These differences were attributed to the greater moisture capacity of the porous materials.

Nissan et al. (18,19,20), using a wind tunnel

designed with continuous air recirculation, studied the mechanism of drying during the falling rate period in three different systems. These systems were wool, polyester fiber and sand, respectively. They made measurements of temperature distribution in these materials and found that after the first falling rate period had been reached, almost the whole bed was at the same temperature. When such structures were drying, the rate of evaporation fell off because heat and water vapor were required to pass through an increasing layer of dry material left by a receding water surface. While this was occurring, a new temperature equilibrium was established within the wet portion. This temperature was called the "pseudo-wet-bulb" temperature.

Nissan, Kaye and Bell (20) developed equations to predict this temperature and the rate of approach to the pseudo-wet-bulb temperature. These equations were based on the assumption that after the drying had proceeded into the falling rate period the vaporization occurred at a liquid surface well within the material.

Ridgway and Callow (21) studied the drying mechanism of an inert, insoluble powder (heavy magnesium carbonate) wetted with different granulating liquids. They showed that there was a linear relationship between the logarithm of the drying rate and the liquid content of the bed over the whole of the falling rate period. They concluded that the operative mechanism in the system that they examined

was the one originally put forward by Filliland (5) and developed later by Nissan, George and Bolles (19).

4. Drying of Pharmaceutical Materials

Cooper et al. (22) discussed the application of the drying theories to the drying of tablet granulations. The granulations are complex systems consisting of many ingredients bonded together by the granulation process. They concluded that the nature of the internal mechanism controlling drying of these materials was similar to that of single-component systems.

5. Solute Migration

Van Krevelen and Hoftijzer (23) dried a single granule of "Nitrochalk"[a] and found that, during the constant rate period, an almost water-impermeable crystalline film was formed around the granule from the dissolved ammonium nitrate. As a result of this film formation, the rate of drying was reduced.

Newitt and Papadopoulos (24) later dried granules of mixed fertilizers and concluded that the mechanicam strength of the final product depended to a large extent upon the location of the material deposited during drying.

Newitt, NaNagara and Papadopoulos (25) subsequently

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[a] A mixed fertilizer produced by Imperial Chemical Industries, Cheshire, England. The composition is given as 48% of calcium carbonate mixed with ammonium nitrate to give 15 1/2% available nitrogen on analysis.

studied the drying of three different grades of sand containing aqueous sodium chloride solution. They found that the solute moved toward the outside of the particles and formed a crust, but they made no quantitative analysis of the resultant distribution. This phenomenon was attributed to the liquid movement in the initial stages of drying.

Higuchi and Kuramoto (26) showed that polyvinylpyrrolidone (PVP), which is used as a binder in the preparation of tablet granulations, was able to form complexes with many of the pharmaceutical substances involved. The authors reported that it might be possible that the non-uniformity of distribution of at least some drugs in granules may parallel the non-uniform distribution of PVP.

Ridgway and Rubinstein (27) studied the radial migration of PVP in spherical granules of magnesium carbonate produced with PVP as the granulating agent. The granules were dried in a drying tunnel and the rate of moisture loss was recorded continuously. They showed that after drying the granules for half an hour, the concentration of PVP in the surface layer rose well above the initial uniform concentration. On the other hand, the concentration in the core declined to below the initial concentration, as shown in Figure 2. By the end of the second falling rate period, the core concentration of PVP was found to increase slightly, with a concomittant decrease in the concentration of PVP at the surface in the same period.

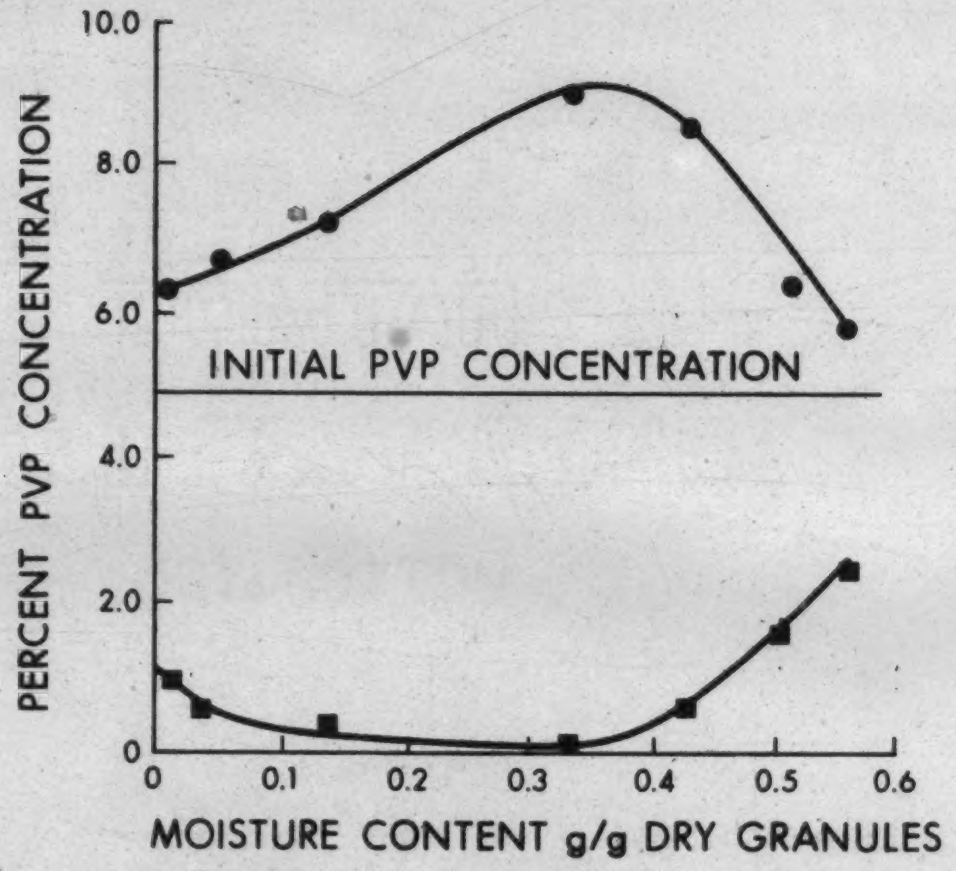

Figure 2

The Variation of PVP Content with Granule Moisture Content
[Adapted from Ridgway and Rubinstein (27)]

● at the surface of the granules
■ in the core of the granules

In order to explain these results they postulated that this change in core concentration occurred due to the "back diffusion" of PVP from the point of the high concentration in the outer surface of the granule to a point of lower PVP concentration in the core. At the final falling rate period of drying the sudden rise in the concentration of PVP in the core was attributed to the receding evaporative interface. With this loss of moisture, the concentration of PVP at the surface remained constant.

More recently Chaudry and King (28) studied the migration of warfarin sodium during the drying of a wet granulation. While the water soluble drug was initially uniformly distributed, the migration of the drug with the solvent during the drying process resulted in an uneven distribution of the medicament in the granulation.

Using thin-layer chromatography, the authors examined the effects of certain tablet additives with a view to inhibiting the migration of sodium warfarin. They found that migration of the drug was reduced to a large extent within the granulation by the addition of calcium phosphate, and the content uniformity of the compressed tablets, when assayed individually, was found to be much improved.

In his work on the migration of dissolved and dispersed substances, Junginger (29,30) indicated that the main parameters affecting the migration of dissolved or

dispersed substances in drying porous materials were the drying rate, surface tension and viscosity of the impregnant. Migration was at a maximum at a drying rate of about ten kilograms per square meter per hour in the system studied. This was a seven layer cloth impregnated with sodium chloride in a methyl alcohol-water system. The movement of moisture followed laws similar to those for diffusion and a method was developed for calculating the final distribution of the impregnant from the moisture distribution during drying.

From this summary of the literature it was clear that the drying process continues to be a subject of interest. This fact alone indicated that the mechanism of moisture movement in powder beds was still not fully understood. Accordingly, it was felt that there was a need for more experimental work on selected pharmaceutical powder systems.

Further study could also be given to the problem of migration of potent drugs during the drying of moist granules. An improved understanding of this phenomenon would aid in ensuring greater uniformity of drug content in certain pharmaceutical preparations. In particular, such information would be of value to the pharmaceutical industry in the formulation of improved compressed tablets.

Objectives of the Present Investigation

The first objective of this investigation was to set up controlled conditions of temperature and air velocity for the drying of damp powder beds, and to measure the physical properties of these beds during drying.

The second objective was to examine quantitatively the migration of a water-soluble solute in these beds. Amaranth was selected as a suitable solute for this purpose. A comparison of the migration pattern of amaranth in beds of lactose (water-soluble) with that occurring in beds of calcium sulfate (water-insoluble) was included in the study.

EXPERIMENTAL

1. Description of Apparatus and List of Materials Used

In order to obtain the necessary data, the study required a tunnel designed to provide air at a constant temperature and velocity, flowing parallel to the exposed upper surface of the bed to be dried. It also required equipment to measure the drying rate, temperature distribution, relative humidity and solute migration. As shown in Figure 3, the main structure of the tunnel was made of asbestos board fastened to a welded steel frame. Satisfactory air flow was achieved through use of a suitable motor driven fan[a].

The air velocity was controlled by using a variable transformer[b], which was connected in series to the fan. Baffle plates were placed at the entrance to the tunnel. Other plates within the calming section and the inclined base immediately up-stream of the powder bed were included in order to reduce fluctuations in the air velocity and to give a uniform air flow free of turbulence in the test section.

The air was heated by nichrome heating coils mounted in the tunnel immediately after the straightening section. Air temperature was controlled by adjusting the voltage

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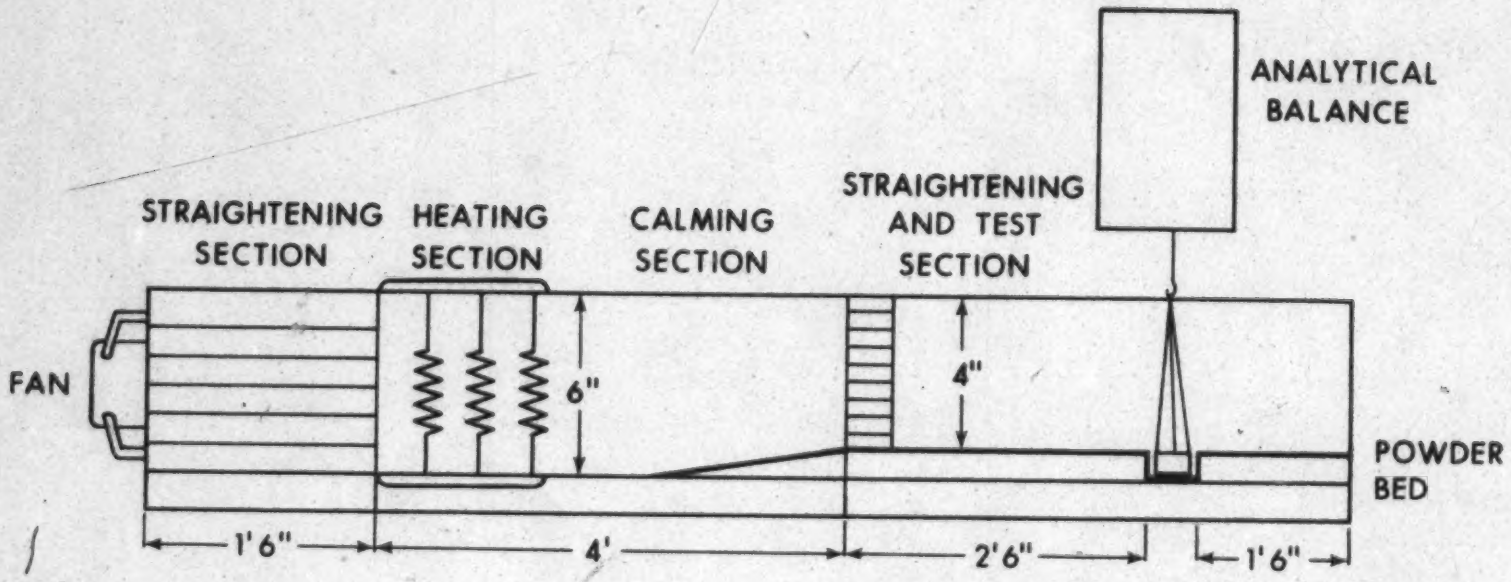
[a] Pamotor model 7500. 115V. 60 Hz. Pamotor Inc., San Francisco

[b] Staco Inc. Model No. 2pf1010 Dayton, Ohio



DRYING TUNNEL

Figure 3

applied to the nichrome coils with a suitable powerstat[a].

For convenience a window was installed in the test section to allow the powder bed to be observed during drying. An analytical balance[b] was placed above the test section and modified to allow attachment of the sample container. This arrangement allowed moisture loss to be determined directly at selected intervals without removal of the sample from the chamber.

The sample was placed in a polystyrene cup[c] of low thermal conductivity. Dimensions of the cup were 5.5 cm for the diameter with the height adjusted to 2.5 cm.

The polystyrene cups used as sample containers were placed in the sample bay of the tunnel with care being taken to place the top of the cup flush with the tunnel floor in order to reduce air flow disturbances from the air passing from the tunnel floor over the bed surface.

The air temperature in the tunnel was measured using calibrated iron-constantan 36 gauge thermocouples[d].

One thermocouple was placed in the calming section and another in the test section just before the powder bed.

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[a] The Superior Electric Co., Bristol, Conn., U.S.A.

[b] Mettler H-20 analytical balance, Model No. 246.

[c] Polymaid cups 67-243 P.C.I., Canada.

[d] Thermo Electric, Brampton, Ontario.

Lactose, B.P.[a], calcium phosphate monobasic[b], calcium sulfate dihydrate[b] and kaolin[a] were the materials used in this investigation. However, on the basis of preliminary examination of each material, lactose and calcium sulfate dihydrate were considered to be most suitable for the purpose of this study.

2. Procedure

A. Calibration of Thermocouples

A calibration curve of the thermocouples was prepared by using an integrating digital voltmeter[c]. The precise evaluation of electromotive force (emf)-temperature relationship of a thermocouple was accomplished by determining its emf output at each of a series of measured temperatures using a standard thermometer[d]. A water bath was used in the calibration procedure. Temperature readings were obtained to a maximum of 70°C, with the reference junction being placed in a vacuum flask containing a well-stirred ice-water mixture.

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[a] The British Drug Houses, Toronto, Canada

[b] Fisher Scientific, New Jersey, U.S.A.

[c] Isotronics Techno-products Ltd., Model No. 350, Ontario, Canada

[d] Range of degrees: -10°C to 200°C, 1° subdivisions, Fisher Scientific, New Jersey, U.S.A.

B. Effect of Conduction of Heat along the Wire to the Junction

A lactose bed containing 35% moisture was prepared by mixing the appropriate amount of lactose and distilled water. The slurry was then poured into a sample container modified by the application of an epoxy[a] coating to the external wall. This coating was employed as an effective vapor barrier. The container was then covered with aluminum foil to prevent evaporation from the surface.

The bed was surrounded by a thick layer of glass wool[b] for further insulation. The bed was left at room temperature and its temperature was measured using two thermocouples.

The experiment was designed so that the lead from the first thermocouple was left at room temperature while the lead from the second thermocouple was placed in the drying tunnel maintained at 58.2°C. As before, the reference junction was placed in a well-stirred ice-water mixture. It was considered that any conduction of heat through the thermocouple lead kept in the heated tunnel would give higher bed temperature readings compared to readings given by that left at ambient temperature. Readings of the bed temperatures were taken every 30 minutes for two hours.

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[a] Epoxy resin, Lepages Ltd., Winnipeg, Canada

[b] 1 1/2 inch thickness

The procedure was then repeated using an unmoistened bed of lactose.

C. Determination of the Humidity of the Air

Air humidity was determined for the most part with the aid of a sling psychrometer[a]. However, a temperature-humidity recorder[b] was later obtained. By using this instrument it was possible to monitor both room temperature and humidity over a period of 24 hours.

D. Determination of the Mean Air Velocity Through the Tunnel at Room Temperature

As outlined by Perry (31) the mean velocity through a rectangular duct could be determined by dividing the cross-section into uniform squares. The velocity at the center of each square was recorded and an average value obtained for the whole duct. For accurate measurements, use was made of a pitot tube[c] connected to a micromanometer[d]. To calculate the air velocity the micromanometer readings were converted to mm of water by referring to a graph supplied with the instrument, taking into consideration the 1:25 slope of the manometer.

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a Taylor Instrument Companies, Rochester, N.Y., U.S.A.

b Brown Recorder, Brown Instrument Division, Philadelphia, U.S.A.

c Prandtl type, James W. Stevenson and Co. Ltd., Ontario, Canada

d James W. Stevenson and Co. Ltd., Ontario, Canada

The air velocity at each point was then calculated using the following formula, which was derived from the Bernoulli equation (32):

$$v = \sqrt{\frac{2g_c h}{\rho}}$$

where v = air velocity in m/sec

g_c = gravitational constant = $9.81 \frac{kg \cdot m}{kg_{wt} \cdot sec^2}$

h = dynamic pressure in $\frac{kg\ force}{m^2}$ = mm of water

ρ = density of the air in $\frac{kg}{m^3}$

The density of the air used was the density of the moist air at room temperature and local barometric pressure of 700 mm Hg (33).

The arithmetic mean and the standard deviation of the air velocity through the tunnel were determined from the 24 readings. The velocity was calibrated against the dial setting on the variable transformer. The air velocity was measured in each drying run at the same selected point, and its value was kept constant. This was done so that the air velocities at the other 23 points would be as close as possible to their original values.

E. Determination of the Permeability of the Powder Bed Container to Water Vapor

Two polystyrene cups were cut to 3.4 cm in height and packed with a lactose slurry containing 33% moisture.

To prevent surface evaporation during heating the cups were covered with aluminum foil and sealed with epoxy resin. The beds were then heated in an oven at 55°C, and loss in weight after 24 hours was determined.

The experiment was repeated using bed containers completely coated with epoxy resin. The loss in weight again was determined after 24 hours' exposure to this temperature. A control was used consisting of an empty coated and sealed container heated in the same manner.

F. Selection of Powders for Study

In selecting powder materials for this study emphasis was placed on ease of handling and suitable physical characteristics. On this basis, lactose was found to be satisfactory as an example of a water-soluble powder.

Selection of a water-insoluble powder proved to be more difficult and involved the examination of kaolin, calcium phosphate and calcium sulfate dihydrate. Kaolin was considered to be unsatisfactory because the powder was very light. As a result, excessive loss in handling was encountered, making it very difficult to withdraw samples accurately. The calcium phosphate powder used in the study proved to have a very slow loss of moisture on drying. For this reason the system was considered to be unsuitable. On the other hand, calcium sulfate dihydrate proved to be

relatively free of such disadvantages and was accordingly chosen for further study.

G. Determination of the Equilibrium Moisture Content (EMC) of the two Systems, Lactose and Calcium Sulfate

The procedure for the determination of loss on drying (LOD) was used to calculate the EMC of lactose and calcium sulfate. U.S.P. specifications for LOD (34,35) were used to dry the samples.

Approximately 2 g of lactose and of calcium sulfate, accurately weighed, were dried to a constant weight at 120°C and 105°C, respectively. The EMC was then calculated by determining the amount of moisture in the sample on a dry basis (36).

H. Preparation of Bed Materials

For the determination of drying rate and temperature distribution, powder beds of lactose and calcium sulfate were prepared by thoroughly mixing 45 gm of the powder with 8 ml of distilled water in a wedgwood mortar. The damp mass was then transferred to the polystyrene cups with the help of a metal spatula to produce a uniform packed bed. Distilled water was used as the wetting agent in this experiment since it is frequently employed in wet granulation procedures.

The percentage of water in the damp mass[a] was chosen to correspond to that required to prepare granules of the material. The time interval between preparation of the powder bed and subsequent installation in the tunnel was less than four minutes in each case.

I. Measurement of Temperature Distribution

The temperature distributions in damp[a] powder beds of both lactose and calcium sulfate were determined. For this purpose iron-constantan thermocouples of 36 gauge wire were employed. One thermocouple was placed at the surface of the powder bed while others were located at depths of 1 cm, 2 cm, and finally at the bottom of the bed. At each of these levels three thermocouples were placed in the bed, one at the center and one glued to the interior of each wall. Figure 4 illustrates the location of the thermocouples in the bed container.

The thermocouples glued to the interior of the wall were placed in their locations in half of the runs from the top of the bed, and in the other half from the bottom of the bed to ensure that heat was not carried through them to the sides of the bed.

J. Measurements of Drying Rate

For the determination of drying rates the prepared

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[a] Final percent moisture in lactose (dry basis), 23.79%. Final percent moisture in calcium sulfate (dry basis), 40.0%.

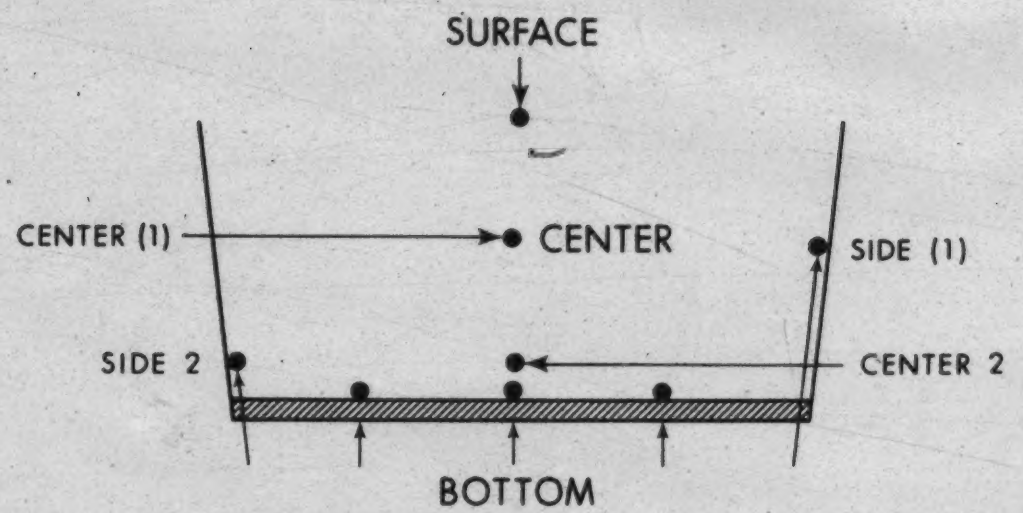

Figure 4

Location of the Thermocouples in the Powder Bed

beds were placed in the sample container. The assembly was hung by thin wires from the pan of a Mettler H-20 analytical balance. Weight measurements were taken every 15 minutes for eight hours, after which the beds were heated in an oven at 105°C to a constant weight.

The data obtained were plotted as a percent of moisture content (dry basis) versus time. The drying rate was determined by taking the difference in moisture content between any two measurements divided by the time period between measurements representing the rate of drying for that time period. These values were plotted against the midpoint of the time periods concerned in order to obtain a drying rate-time curve. Similarly, the same values were plotted against the midpoint of the moisture content values for a drying rate-moisture content curve (37).

K. Solute Migration Determination

i. Apparatus

The apparatus for determining the concentration of the migrated dye through the powder bed consisted of three units.

a. An SP 600 (series II) spectrophotometer[a] which was designed to carry out single beam absorptiometric measurements within the wavelength range 340-1000 nm.

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[a] Pye Unicam Ltd., York Street, Cambridge, England

b. An automatic sample changer[a] which was designed as an accessory for the SP 600. The changer held up to 50 samples and transferred them one at a time into the sample cell of the spectrophotometer.

After a sample was read it was drained from the holder by suction and replaced automatically by the next sample. This operation was repeated until the last sample had been measured.

c. A recorder. A suitable strip chart recorder[b] was employed for readout purposes.

ii. Procedure

The method employed in this investigation was to prepare beds of lactose and calcium sulfate dampened with known amounts of an aqueous amaranth[c] solution, and to subject the beds to drying under a current of air at constant temperature and velocity. The drying could be stopped at any point and the solute migration and moisture distribution could be determined by analysis of samples taken from various levels in the bed.

Damp beds of lactose and of calcium sulfate were prepared by moistening 45 g of the powder in question with

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[a] Pye Unicam Ltd., York Street, Cambridge, England

[b] Varicord Model 43, Photovolt Corp. New York City, U.S.A.

[c] The British Drug Houses, Toronto, Canada

eight ml of 0.088% aqueous amaranth solution. Each system was triturated quickly in a mortar to produce a uniformly wetted mass. The mixture was then transferred to the bed container and exposed to standardized drying conditions.

The drying process was stopped at different times, and six samples from the bed were taken each time by using a lathe-milling machine[a]. Milling was done by using a two fluted, 0.5 inch diameter milling head.

a. Method of Sampling

A suitable jig was prepared to allow accurate centering of the container on the milling machine table in each determination.

This arrangement made it possible to obtain subsequent samples from the same area of the bed involved. In sampling a bed, six fractions were removed from the same hole, each succeeding fraction representing a deeper penetration into the hole.

Accurate control of fraction depths was made possible through the use of a micrometer attachment. By adjusting this device it was possible to manually guide the milling head to a predetermined depth. Table I shows the established levels in the powder beds from which each sample fraction was taken.

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[a] Maximat 7, Canadian Edelstaal, Scarborough, Ontario, Canada

Table I

Established Levels in the Powder Bed for Sampling

Distance from the surface in cm	Distance from the surface in percent
0.1587	7.14
0.3175	14.28
0.6350	28.57
1.2700	57.14
1.9050	85.71
2.2220	100.00

The moisture content of each sample was determined gravimetrically. A 150 mg portion was then weighed out from each sample and dissolved in 10 ml of distilled water. In dealing with the insoluble calcium sulfate, the colored solutions were centrifuged to obtain a clear supernatant. The concentration of amaranth in these samples was then determined by measuring the percent transmittance at 522.5 nm.

b. Determination of Calibration Curve for Amaranth Solution

A solution of 0.009 g of amaranth in 100 ml distilled water was prepared from a stock solution containing 0.9 g of amaranth. Of this 20 ml was diluted to 100 ml with more distilled water to form a stock solution.

Ten dilutions of 10 ml each were then prepared as shown in Table II.

Table II

Preparation of Amaranth Solutions for Calibration Curve

Stock Solution Used in ml	Concentration of Amaranth In the Final Solution in Percent
1	0.18×10^{-3}
2	0.36×10^{-3}
3	0.54×10^{-3}
4	0.72×10^{-3}
5	0.90×10^{-3}
6	1.08×10^{-3}
7	1.26×10^{-3}
8	1.44×10^{-3}
9	1.62×10^{-3}
10	1.80×10^{-3}

The percent transmittance was measured using the SP 600 spectrophotometer and the recorder readout. From these readings the absorbance for each solution was then calculated. A curve was prepared of the concentration of the dye versus the absorbance. This curve was used to determine the concentration of the dye samples.

c. Stability of Amaranth Solution

Two grams of lactose and of calcium sulfate were mixed with amaranth 0.088% solution as described previously. These powders, as well as a sample of 0.088% amaranth solution, were heated for 60 hours in an oven set at 55°C. An unheated sample of this amaranth solution was employed as a control.

After the heating period, the powders were dispersed in 100 ml of distilled water. In dealing with the insoluble calcium sulfate, the colored solutions were centrifuged to obtain a clear supernatant. One ml of each solution was then diluted to 10 ml with distilled water, and the concentration of each solution was then determined.

d. Determination of the Effect of Lactose on Absorbance of Amaranth

The effect of lactose on the absorbance of amaranth was tested by the addition of lactose to a known concentration of amaranth. The concentration of lactose was chosen to correspond approximately to that which would be present in the final solution used for determining amaranth

concentration in the bed samples. Accordingly two solutions of 0.0013% amaranth were prepared in distilled water and in 1% lactose solution, respectively. The absorbance of these solutions was then measured at a wavelength of 522.5 nm. Data obtained were treated statistically to determine the significance.

Preliminary determinations were done to establish the wavelength at which maximum absorption occurred. This was achieved by using a known concentration solution of amaranth and recording the absorbance at various wave lengths.

RESULTS

1. Calibration Curve of Thermocouples

Each thermocouple was calibrated individually. The emf-temperature relation of the iron-constantan thermocouple used in this work is shown in Table III. The plot of the mean emf against temperature gave a linear curve in the 0°C - 70°C range as shown in Figure 5.

2. Effect of Conduction of Heat along the Wire to the Junction

The temperature readings of an insulated bed of moistened lactose are shown in Table IV. Analysis of variance of the data showed no significant difference (at the 5% level) in the thermocouple readings due to the difference in procedures used.

To investigate the possible effect of water acting as a heat conductor, the test was repeated using an unmoistened bed of lactose. The results are shown in Table V. Analysis of variance of the data showed no significant difference (at the 5% level) between the thermocouple leads.

3. Measurement of Air Humidity

Calculation of the relative humidity was necessary for the part of the work where a sling psychrometer was used since the barometric pressure was lower than 760 mm Hg. Corrections were applied to the values of absolute humidity determined from the wet-bulb and dry-bulb temperature

Table III

EMF-Temperature Relation of Iron-Constantan Thermocouples

Temperature (°C)	Emf in Millivolt			
	Run I[a]	Run II[b]	Run III[c]	Mean
0	0.002	0.002	0.002	0.002
5	0.253	0.255	0.253	0.253
10	0.501	0.502	0.500	0.501
15	0.752	0.753	0.751	0.752
20	1.029	1.028	1.030	1.029
25	1.274	1.275	1.273	1.274
30	1.542	1.543	1.541	1.542
35	1.796	1.794	1.795	1.795
40	2.065	2.067	2.066	2.066
45	2.319	2.320	2.321	2.320
50	2.580	2.582	2.581	2.581
55	2.840	2.838	2.839	2.839
60	3.111	3.113	3.112	3.112
65	3.363	3.361	3.362	3.362
70	3.622	3.624	3.623	3.623

a,b,c Represent the mean value of eleven thermocouples calibrated in each run

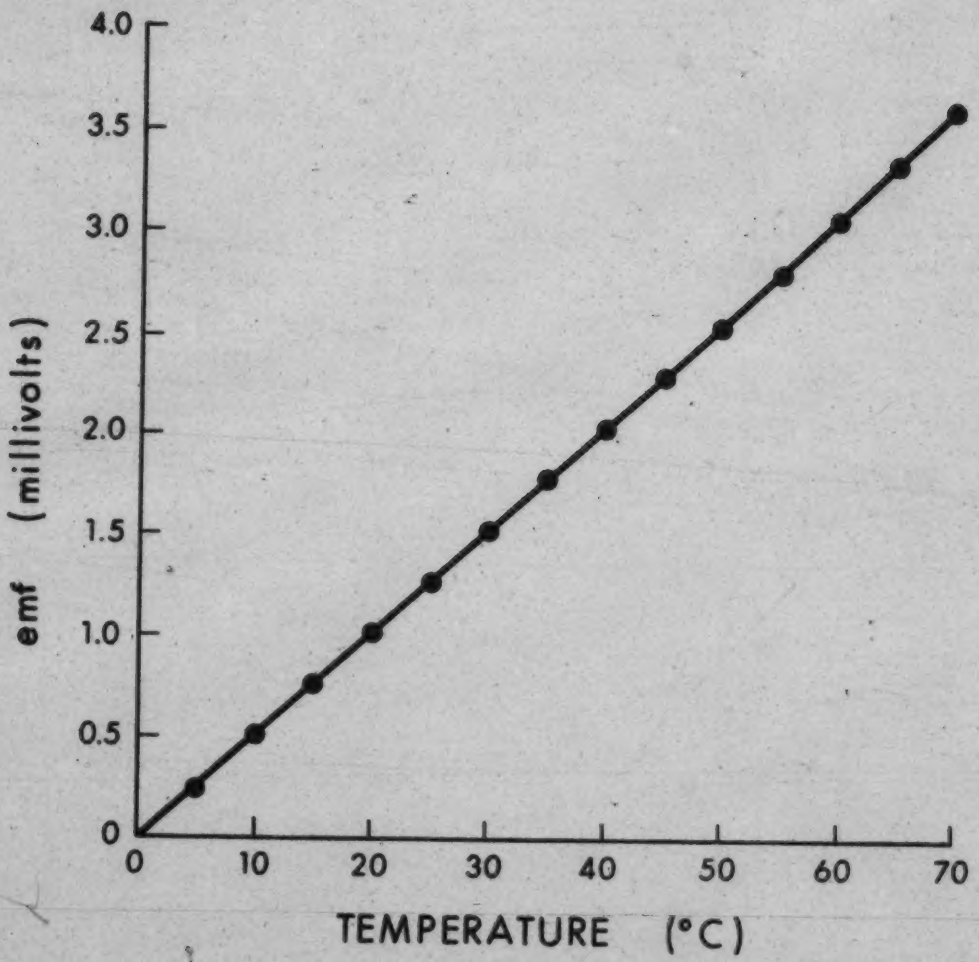

Figure 5

Calibration Curve for Iron-Constantan Thermocouples

Table IV

Temperature Readings as a Function of Time Obtained with Moistened[a] Lactose Bed

Time (Min)	Thermocouple No. 1[b] Temperature (°C)			Thermocouple No. 2[c] Temperature (°C)		
	Run I	Run II	Mean	Run I	Run II	Mean
0	26.80	27.00	26.90	26.80	27.00	26.90
30	27.00	27.60	27.30	27.00	27.60	27.30
60	27.10	27.60	27.35	27.10	27.65	27.38
90	27.00	27.65	27.33	27.10	27.65	27.38
115	27.00	28.20	27.60	27.10	28.20	27.65
145	27.00	28.25	27.63	27.00	28.40	27.70
165	27.00	28.50	27.75	27.10	28.50	27.80
190	27.05	29.00	28.03	27.10	29.00	28.05

[a] Moisture content 35.1% (dry basis)

[b] The lead of thermocouple No. 1 was left at ambient temperature 28°C

[c] The lead of thermocouple No. 2 was placed in the tunnel at 58.2°C

Table V

Temperature Readings as a Function of Time Obtained with Unmoistened Lactose Bed

Time (Min)	Thermocouple No. 1[a] Temperature (°C)			Thermocouple No. 2[b] Temperature (°C)		
	Run I	Run II	Mean	Run I	Run II	Mean
0	27.60	27.40	27.50	27.50	27.50	27.50
30	27.80	27.60	27.70	27.60	27.80	27.70
60	28.30	28.40	28.20	28.25	28.15	28.20
90	28.60	28.40	28.50	28.45	28.55	28.50
115	28.65	28.45	28.55	28.50	28.60	28.55
145	28.65	28.75	28.70	28.55	28.75	28.70
165	29.20	29.00	29.20	29.30	29.10	29.20
190	29.25	29.35	29.30	29.30	29.30	29.30

[a] The lead of thermocouple No. 1 was left at ambient temperature 28°C

[b] The lead of thermocouple No. 2 was placed in the tunnel at 58.2°C

readings. The method of calculation used has been described by Perry (31). The absolute humidity values were corrected to the required barometric pressure. To do so the following expressions were defined.

t = dry-bulb temperature (°F);

t_w = wet-bulb temperature (°F);

P = barometric pressure in inches of mercury;

ΔP = pressure difference from standard barometric pressure in inches of mercury;

H = moisture content of air in grains/lb dry air;

H_s = moisture content of air saturated at the wet-bulb temperature t_w in grains/lb dry air;

ΔH = moisture content correction of air when barometric pressure differs from standard barometer, in grains/lb dry air;

ΔH_s = moisture content correction of air saturated at the wet-bulb temperature when barometric pressure differs from standard barometer, in grains/lb dry air.

The ΔH values were obtained by reducing ΔH_s[a] value by one percent when $t - t_w = 24°F$. When the difference between the dry-bulb and the wet-bulb temperature was other than 24°F, the ΔH_s value was corrected proportionally, and ΔH

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[a] ΔH_s value taken from Table 15-2 at t_w, and ΔP, page 15-8, Reference 31

values were calculated as follows:

$$\Delta H = \Delta H_s \left[1 - \frac{t-t_w}{24} \times 0.01 \right]$$

To obtain the absolute humidity value at corrected pressure (H_c), the following expression was used:

$$H_c = H + \Delta H$$

The value of H was obtained from a standard chart[a].

Similarly, relative humidity values were determined from the partial pressure of water in the mixture and from the vapor pressure of water vapor. The partial pressure of water was calculated assuming ideal gas behavior as

$$p = \frac{H_c P_t}{(Mw/Ma) + H_c}$$ [a]

where p = partial pressure of water vapor in inches of mercury;

P_t = total pressure of water vapor in inches of mercury;

H = absolute humidity in pounds per pound dry air corrected to the actual pressure;

Ma = "molecular weight" of air (lb/lb mole)

Mw = "molecular weight" of water vapor (lb/lb mole)

The relative humidity (RH) was obtained by dividing the calculated partial pressure by the vapor pressure of water

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[a] Page 15-13, Reference 31

at the dry-bulb temperature.

$$\text{Relative humidity (RH)} = \frac{100p}{p_s}$$

4. Determination of Mean Air Velocity Through the Drying Tunnel at Room Temperature

The micromanometer readings in mm of water obtained in determining the air velocity through the tunnel are shown in Table VI.

The average of the three determinations was then plotted to show the locations of these readings in the cross-sectional area of the tunnel (Figure 6).

The air velocity was then calculated from the following formula:

$$v = \sqrt{\frac{2g_c h}{\rho}}$$

The mean velocity was 3.4 m/sec (or 11.2 ft/sec). In preliminary velocity determinations, the readings in the central part of the tunnel were higher than those found at the sides of the tunnel. A more uniform distribution of air was then obtained by inserting a shaped baffle into the air stream between the fan and the tunnel. The air velocity for each run was determined at a selected point in the center of the tunnel which represented one of the 24 squares. The air velocity at this point was kept constant at its original value by adjusting the variable transformer.

Table VI

Micromanometer Readings in mm of Water
Through the Cross-sectional Area of the Tunnel

Locations of Readings	Micromanometer Readings in mm of Water			
	Run I	Run II	Run III	Mean
1	0.60	0.64	0.62	0.62
2	0.68	0.70	0.66	0.68
3	0.60	0.62	0.64	0.62
4	0.58	0.59	0.63	0.60
5	0.58	0.59	0.57	0.58
6	0.58	0.58	0.58	0.58
7	0.67	0.69	0.68	0.68
8	0.69	0.70	0.68	0.69
9	0.70	0.70	0.70	0.70
10	0.69	0.69	0.69	0.69
11	0.72	0.69	0.69	0.70
12	0.68	0.66	0.64	0.66
13	0.64	0.62	0.66	0.64
14	0.70	0.68	0.69	0.69
15	0.70	0.72	0.68	0.70
16	0.70	0.68	0.69	0.69
17	0.74	0.74	0.74	0.74
18	0.69	0.69	0.69	0.69
19	0.60	0.60	0.60	0.60
20	0.62	0.62	0.63	0.62
21	0.60	0.60	0.60	0.60
22	0.60	0.60	0.60	0.60
23	0.68	0.69	0.67	0.68
24	0.62	0.63	0.61	0.62

1 0.62	2 0.68	3 0.62	4 0.60	5 0.58	6 0.58
7 0.68	8 0.69	9 0.70	10 0.69	11 0.70	12 0.66
13 0.64	14 0.69	15 0.70	16 0.69	17 0.74	18 0.69
19 0.60	20 0.62	21 0.60	22 0.60	23 0.68	24 0.62

Figure 6

Cross-sectional Area of the Tunnel
with Corresponding Readings in Each Square[a]

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[a] Micromanometer readings in mm of water in the center of each square. Area of each square = 1 square inch.

5. Determination of the Permeability of the Bed Container to Water Vapor

Lactose slurries containing 33% moisture were placed in sealed uncoated containers and in sealed containers coated with epoxy resin. Each sample was heated in an oven for 24 hours at a temperature of 55°C. The control consisted of an empty uncoated cup. The weight losses are shown in Table VII.

Table VII

Weight Losses in Percent of Sealed Lactose Beds[a] on Heating at 55°C for 24 Hours

Sample	Control Loss	Sealed Uncoated Bed Containers	Sealed Epoxy Resin Coated Containers
1	0.125	8.200	0.921
2	0.125	8.192	0.950
3	0.115	8.293	1.051

[a] Moisture content 33% (dry basis)

From a study of the values presented in the above table it was clear that the use of an epoxy resin coating for the cup was responsible for the great reduction in

weight loss obtained. Reference to published thermal conductivity values for both polystyrene and epoxy resin indicated that the resin could have no effect on the insulating effect of the container[a]. The results suggest that the resin operated by rendering the polystyrene cup less permeable to water vapor from the lactose slurry.

6. Equilibrium Moisture Content and Final Moisture Content of Lactose and Calcium Sulfate

The equilibrium moisture content (EMC) in lactose and calcium sulfate dihydrate as determined by the U.S.P. loss on drying method (34,35) and calculated on dry basis (36) are shown in Table VIII. The anhydrous form of both lactose and calcium sulfate was obtained as a result of drying. The final moisture content in lactose and calcium sulfate beds after mixing eight ml of distilled water with 45 gm of the powder is also shown in Table VIII.

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[a] Thermal conductivity of polystyrene is equal to 0.058 - 0.09 Btu/hr ft^2 F° ft (31), pages 23 - 55; that of epoxy resin is equal to 0.10 - 0.80 Btu/hr ft^2 F° ft (31), pages 23 - 54.

Table VIII

The Equilibrium Moisture Content
and the Final Moisture Content
in Beds of Lactose and Calcium Sulfate

Material	Equilibrium Moisture Content (%)				Percent Final Moisture Content (dry basis)
	Run I	Run II	Run III	Mean	
Lactose B.P.	5.11	5.22	5.01	5.11	23.79
Calcium Sulfate Dihydrate	18.69	18.99	18.99	18.89	40.00

7. Temperature Distribution

The results of temperature distribution in moistened beds of lactose and calcium sulfate are shown in Tables IX - XIV. At least four determinations were made for each system. Figures 7 - 12 show the temperature distribution in these beds using data obtained from thermocouples located as shown in Figure 4.

A study of the temperature distribution through a moistened bed of lactose with one side insulated showed that during the first 30 minutes heat was transferred through the uninsulated wall from outside to inside. The temperature in the sample well was 44°C during the run. It would appear from Figure 10 that after about 90 minutes the heat was lost to the surroundings.

Figures 7, 8 and 9 represent temperature distribution in moistened beds of lactose. The temperature in the center of the bed was always lower than the temperature at the wall in both levels, in the uninsulated bed container (Figure 7).

In the case of the resin-coated beds and the coated and insulated beds, the temperature at the wall was lower than that at the center for the first two hours, after which it started to level out with the center temperature. This could be due to the insulation of the bed which reduced heat loss to the surroundings.

The surface thermocouple in Figure 7 apparently was misplaced, since it is obvious from the high starting

Table IX

Temperature Distribution in an Uninsulated Moistened Bed of Lactose BP[a]
(Readings in °C)

Time (Min)	Position in Powder Bed					
	Side 1	Center 1	Side 2	Center 2	Surface	Bottom Center
0	27.6	24.3	25.5	24.8	38.8	30.0
30	38.8	34.8	36.7	33.7	43.8	34.0
60	43.8	39.0	41.5	38.9	47.3	37.2
90	45.0	43.0	43.5	42.3	48.3	38.9
120	45.8	44.2	44.5	43.4	48.5	39.5
150	46.4	44.7	45.0	44.2	48.7	40.2
180	46.5	45.2	45.6	44.6	49.0	40.6
210	46.6	45.5	45.8	44.8	49.4	41.3
240	47.0	45.8	46.0	45.0	49.5	41.9
270	47.2	45.8	46.2	45.5	49.5	42.3
300	47.4	46.2	46.5	45.6	49.6	42.4
330	47.2	46.2	46.5	45.6	49.6	43.0
360	47.4	46.1	46.2	45.6	49.7	43.5
390	47.6	46.4	46.6	45.7	49.8	43.6
420	47.7	46.5	46.6	45.8	49.8	44.0

[a] Operating conditions were: Room temperature, 30°C; Tunnel temperature, 54°C ± 1°; Air velocity, 11.2 ft/sec; Moisture content, 23.8%

Table X

Temperature Distribution in a Moistened Lactose Bed Using Container Coated with Epoxy Resin and Insulated with Glass Wool[a]

(Readings in °C)

Time (Min)	Position in Powder Bed							
	Side 1	Center 1	Side 2	Center 2	Surface A	Surface B	Bottom Center	Between Glass Wool
0	20.0	19.5	20.0	19.5	19.5	19.3	20.0	27.8
30	23.0	22.8	24.2	22.8	26.0	25.7	21.5	26.5
60	27.8	27.3	27.8	27.0	30.7	30.5	24.5	28.5
90	32.5	31.9	31.8	31.4	34.7	35.0	27.5	30.0
120	36.0	35.5	35.0	35.0	37.8	38.0	32.0	31.3
150	37.7	37.2	37.0	37.0	39.3	39.3	34.0	32.5
180	39.4	39.0	38.4	38.5	40.8	40.8	36.5	33.5
210	40.3	40.0	39.6	39.6	41.6	41.6	37.3	34.0
240	41.0	40.7	40.0	40.4	42.3	42.3	37.8	34.5
270	41.3	41.0	40.4	40.6	42.5	42.5	38.5	35.0
300	42.0	41.6	41.0	41.3	43.0	43.0	38.9	35.3
330	42.3	42.0	41.3	41.5	43.3	43.3	39.0	35.4
360	42.5	42.4	41.5	42.0	43.7	43.6	39.5	35.6
390	43.0	42.5	42.2	42.3	44.0	44.0	39.7	35.7
420	43.2	43.0	42.5	42.6	44.2	44.2	40.2	38.1

[a] Operating conditions were: Room temperature, 22°C; Tunnel temperature, 54°C ± 1°; Air velocity, 11.2 ft/sec; Moisture content, 23.8%

Table XI

Temperature Distribution in a Moistened Lactose Bed Using a Container Coated with Epoxy Resin Only[a] (Readings in °C)

Time (Min)	Position in Powder Bed					
	Side 1	Center 1	Side 2	Center 2	Surface	Bottom Center
0	25.5	22.0	25.5	23.8	22.4	27.0
30	38.9	37.8	34.5	34.5	39.7	30.5
60	43.2	43.0	41.0	41.5	44.0	33.6
90	45.3	45.0	43.7	43.3	46.0	36.5
120	46.0	46.0	45.0	44.5	46.2	38.5
150	46.3	46.1	45.6	45.6	46.6	41.0
180	47.3	47.0	46.5	46.5	47.4	42.0
210	47.6	47.6	47.0	47.0	48.0	42.5
240	48.4	48.0	47.3	47.5	48.5	42.6
270	48.4	48.5	47.5	47.5	48.5	42.6
300	48.5	48.5	47.6	47.5	48.6	42.6
330	48.6	48.6	47.6	47.6	48.6	42.0
360	48.6	48.7	47.8	47.7	49.0	42.8
390	48.7	48.7	48.1	48.1	49.0	43.1
420	48.9	48.8	48.2	48.2	49.1	43.3

[a] Operating conditions were: Room temperature, 24°C; Tunnel temperature, 54°C ± 1°; Air velocity, 11.2 ft/sec; Moisture content, 23.8%

Table XII

Temperature Distribution in a Moistened Lactose Bed Contained in a Polystyrene Cup, One half Uninsulated, the Other Half Coated with Epoxy Resin and Insulated with Glass Wool[a]

(Readings in °C)

Time (Min)	Insulated Container Half				Coated and Insulated Container Half		Surface Temperature	Bottom Temperature
	Side 1	Center 1	Side 2	Center 2	Side 1	Side 2		
0	25.1	24.8	25.5	23.8	24.5	25.0	23.3	23.5
30	34.5	33.5	33.5	32.5	37.0	33.5	43.4	27.3
60	41.1	38.2	40.2	39.7	42.5	40.2	47.0	31.5
90	43.7	43.1	42.8	42.5	45.0	42.6	48.5	37.0
120	45.3	45.0	44.2	44.5	46.5	44.7	49.5	38.0
150	46.5	46.2	45.6	46.0	47.5	46.0	50.0	40.5
180	47.3	47.0	46.6	46.6	48.2	46.9	50.8	41.5
210	48.0	47.9	47.2	47.5	48.6	47.8	50.1	42.5
240	48.0	47.9	47.2	47.5	48.5	47.9	50.0	43.2
270	48.1	48.0	47.5	47.8	48.9	48.0	50.4	45.0
300	48.4	48.3	47.6	48.0	49.0	48.3	50.5	45.6
330	48.5	48.5	48.0	48.5	49.0	48.5	50.5	45.9
360	48.6	48.6	48.0	48.6	49.1	48.6	50.8	46.0
390	48.7	48.7	48.2	48.6	49.3	48.7	50.8	46.2
420	48.8	48.8	48.4	48.7	49.3	48.7	50.8	46.6

[a] Operating conditions were: Room temperature, 26°C, Tunnel temperature, 54°C ± 1°; Air velocity, 11.2 ft/sec; Moisture content, 23.8%

Table XIII

Temperature Distribution in a Moistened Calcium Sulfate Dihydrate Bed[a]

(Readings in °C)

Time (Min)	Position in Powder Bed						
	Side 1	Center 1	Side 2	Center 2	Surface A	Surface B	Bottom Center
0	27.4	24.3	25.6	26.2	25.9	25.3	28.0
30	32.0	28.9	31.5	31.1	29.0	28.5	28.8
60	34.9	33.0	33.5	32.6	32.0	31.6	29.5
90	36.3	34.8	35.5	35.3	36.6	36.3	30.5
120	37.2	36.0	36.3	36.4	38.0	37.9	35.5
150	37.8	36.9	37.3	37.2	39.6	39.0	34.0
180	38.1	37.1	37.3	37.4	40.6	39.9	35.2
210	38.9	37.9	37.8	37.8	41.9	40.8	36.0
240	39.6	38.1	38.2	38.1	42.6	41.6	36.2
270	40.4	38.3	38.9	38.2	43.2	42.1	26.6
300	41.0	38.6	39.7	39.5	43.7	42.9	37.0
330	41.6	39.3	40.0	39.8	44.2	43.4	37.5
360	42.3	40.0	40.7	40.0	44.5	43.8	37.6
390	42.6	41.9	41.6	41.1	44.6	43.9	37.8
420	43.8	43.8	42.9	42.8	45.6	45.6	38.0

[a] Operating conditions were: Room temperature, 26°C; Tunnel temperature, 54°C ± 1°; Air velocity, 11.2 ft/sec; Moisture content, 40.0%

Table XIV

Temperature Distribution in a Moistened Calcium Sulfate Dihydrate Bed[a]
(Readings in °C)

Time (Min)	Position in Powder Bed					
	Side 1	Center 1	Side 2	Center 2	Surface	Bottom Center
0	28.0	25.0	29.0	25.9	25.3	28.0
30	32.0	25.9	31.5	26.9	28.4	28.5
60	34.5	32.0	33.0	30.9	31.5	29.0
90	36.5	34.8	35.0	35.9	34.2	30.5
120	37.2	35.9	36.0	35.9	36.1	31.5
150	37.9	36.0	37.0	36.0	37.9	32.5
180	38.5	37.3	38.2	36.9	39.8	34.1
210	39.0	37.9	38.9	37.9	40.5	35.0
240	39.6	38.2	39.5	38.1	41.5	35.9
270	40.5	38.5	39.9	39.6	42.2	36.0
300	40.9	39.6	40.5	40.0	42.9	36.5
330	41.6	41.0	40.9	40.4	43.4	37.0
360	42.5	42.0	41.0	40.8	43.8	37.5
390	42.7	42.5	42.2	41.5	44.8	38.0
420	43.8	43.8	43.0	42.9	45.5	38.5

[a] Operating conditions were: Room temperature, 28°C; Tunnel temperature, 54°C ± 1°; Air velocity, 11.2 ft/sec; Moisture content, 40.0%

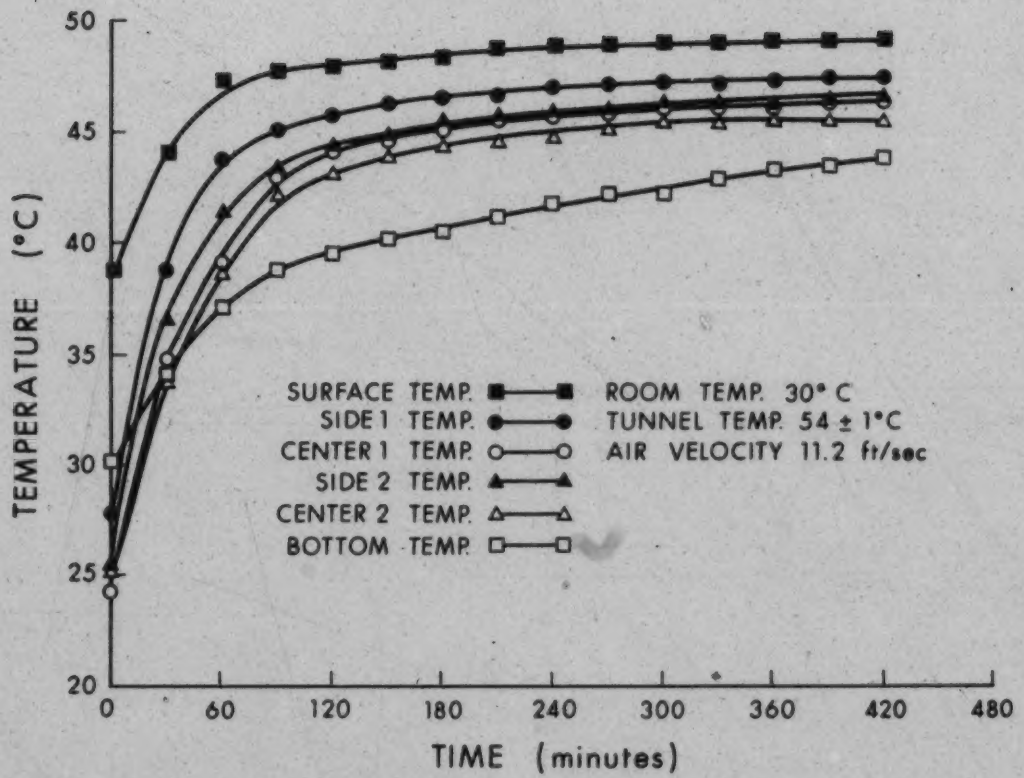

Figure 7

Temperature Distribution in a Moistened Lactose Bed
Using an Uninsulated Container

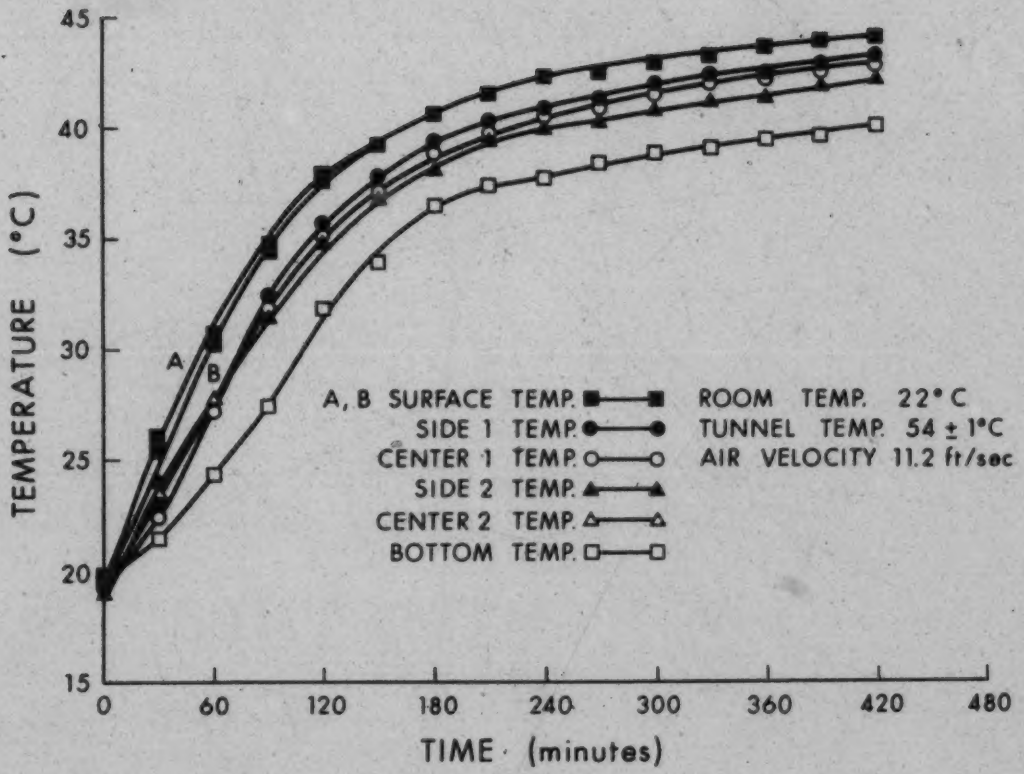

Figure 8

Temperature Distribution in a Moistened Lactose Bed
Using Container Coated with Epoxy Resin
and Insulated with Glass Wool

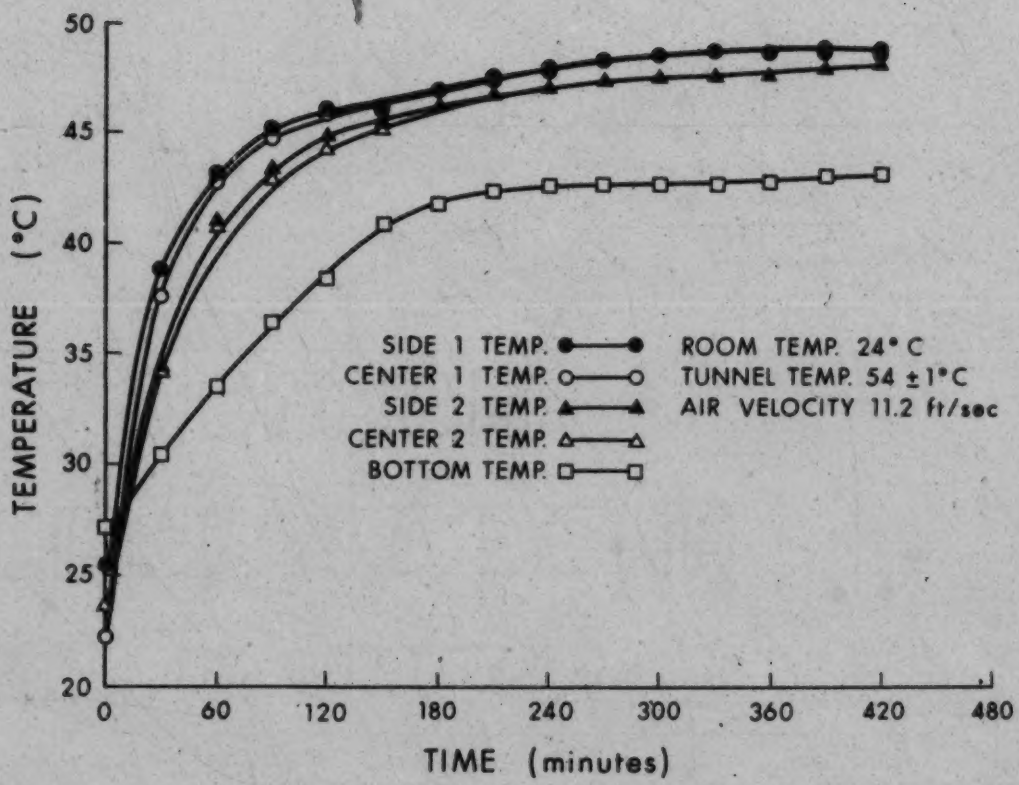

Figure 9

Temperature Distribution in a Moistened Lactose Bed
Using Container Coated with Epoxy Resin Only

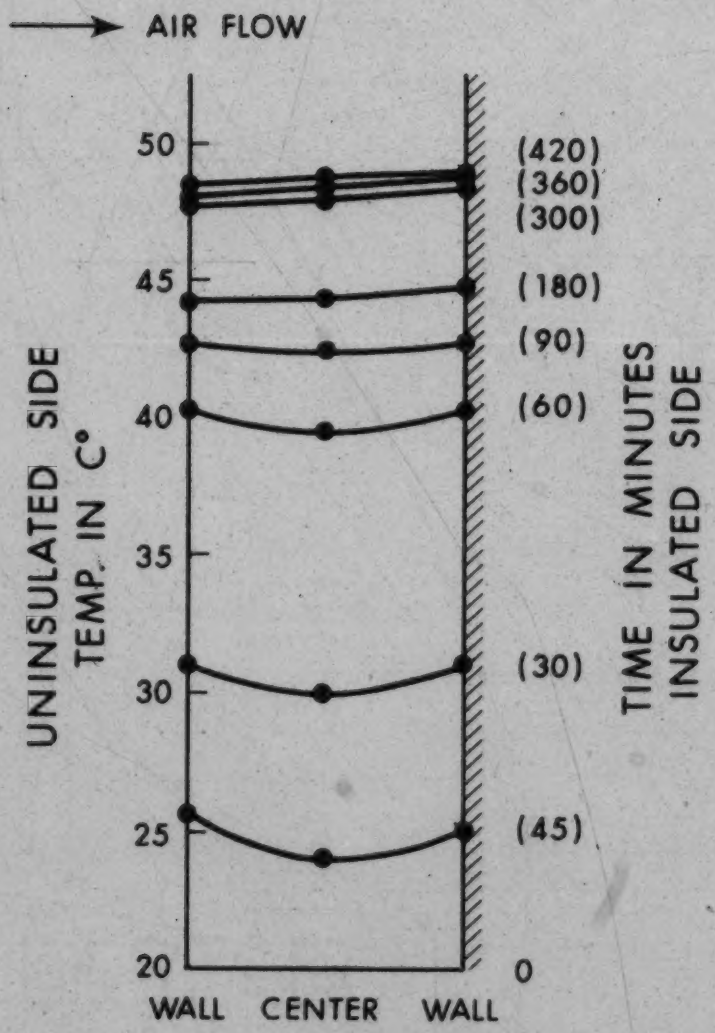

Figure 10

Temperature Distribution in a Moistened Lactose Bed
Using Container Half Coated with Epoxy Resin
and Insulated with Glass Wool

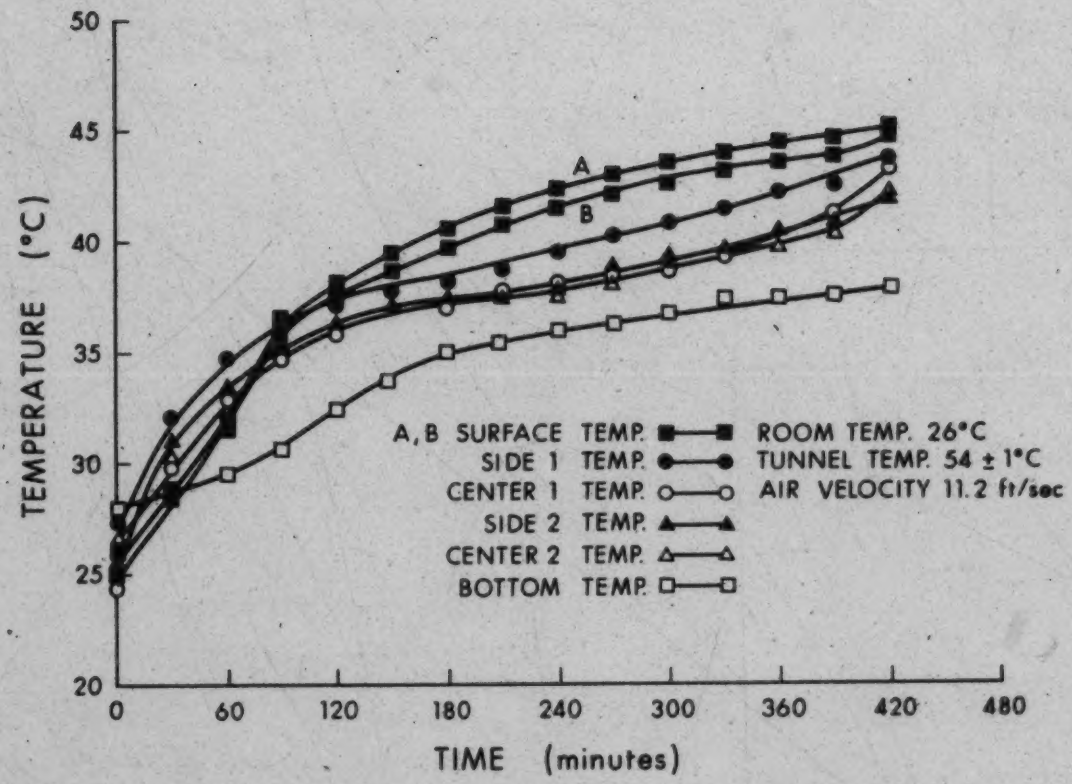

Figure 11

Temperature Distribution in a Moistened Calcium Sulfate Dihydrate Bed Using Container Coated with Epoxy Resin Only

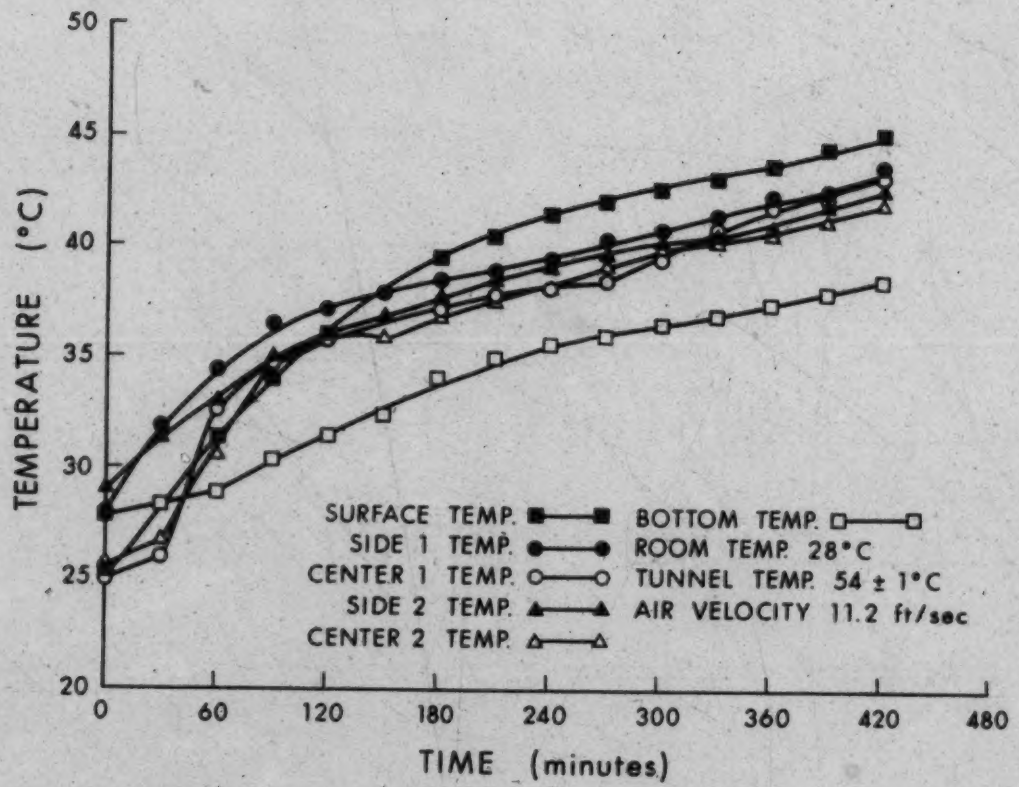

Figure 12

Temperature Distribution in a Moistened Calcium Sulfate Dihydrate Bed Using Container Coated with Epoxy Resin Only

temperature that it was above the plane where vaporization took place.

The temperature distribution in moistened beds of calcium sulfate dihydrate using resin coated containers is shown in Figures 11 and 12. A comparison of these values with those contained in Figure 9 indicates that the temperature in the calcium sulfate bed varied a great deal more than in a lactose bed. Also, the surface temperature in the calcium sulfate bed was lower than the temperature recorded at the different locations in the bed in the first hour of the drying process.

8. Drying Rate

The results of four drying runs for beds of lactose and those of two runs for calcium sulfate are reported in the following pages. All runs were made under the same drying conditions. The air temperature was maintained at 54°C±1° with a velocity of 11.2 ft/sec, and relative humidity of 40 percent.

A. Drying Rate Curves

The data obtained were collected and are presented in Tables XV - XX. These values were employed in the construction of moisture content versus time plots and drying rate curves (Figures 13 - 21).

The drying rate curves were obtained from the graph of moisture content versus time, by taking the difference

Table XV

Percent Moisture in Damp Powder Beds of Lactose Versus Time[a]

Time	Percent Moisture Content Calculated on Basis of Dry Weight				
	Run I	Run II	Run III	Run IV	Mean
0 Min	23.90	23.23	23.85	23.45	23.61
15 Min	22.48	22.07	22.15	22.35	22.26
30 Min	21.46	21.48	21.44	21.71	21.52
45 Min	20.48	20.60	20.70	20.84	20.65
60 Min	19.84	19.79	19.83	20.03	19.87
75 Min	19.07	19.23	19.10	19.41	19.18
90 Min	18.53	18.64	18.59	18.82	18.65
105 Min	18.25	18.09	18.03	17.95	18.08
120 Min	17.42	17.51	17.50	17.42	17.46
135 Min	17.00	17.17	17.10	17.12	17.12
150 Min	16.63	16.66	16.66	16.77	16.68
165 Min	16.02	16.32	16.09	16.48	16.23
180 Min	15.83	16.03	16.03	16.19	16.02
195 Min	15.58	15.68	15.62	15.90	15.70
210 Min	15.32	15.26	15.26	15.41	15.31
225 Min	14.89	14.96	14.92	15.09	14.97
240 Min	14.66	14.88	14.80	14.74	14.77
255 Min	14.48	14.63	14.65	14.56	14.58
270 Min	14.24	14.32	14.30	14.20	14.28
285 Min	14.02	14.07	14.10	14.16	14.09
300 Min	13.59	13.77	13.75	14.13	13.81
315 Min	13.50	13.60	13.59	13.61	13.58
330 Min	13.41	13.47	13.41	13.42	13.43
345 Min	13.24	13.22	13.23	13.29	13.25
360 Min	12.99	12.97	12.98	12.96	12.98
375 Min	12.82	12.88	12.77	12.76	12.81
390 Min	12.70	12.63	12.65	12.60	12.65
405 Min	12.50	12.40	12.42	12.40	12.43
420 Min	12.25	12.20	12.23	12.20	12.22
24 Hr				10.80	
74 Hr				5.74	
294 Hr				5.12	

[a] Operating conditions were: Tunnel temperature, 54°C ± 1°; Air velocity, 11.2 ft/sec; Relative humidity, 40%

Table XVI

Moisture Content[a] and Drying Rate in Beds of Lactose[b]

Time (Min)	Run I		Run II	
	Percent Moisture	Drying Rate (g/min)	Percent Moisture	Drying Rate (g/min)
7.5	23.10	0.095	22.50	0.077
15	22.48	0.081	22.07	0.070
30	21.46	0.062	21.48	0.052
45	20.48	0.054	20.60	0.044
60	19.84	0.046	19.79	0.043
90	18.53	0.040	18.04	0.036
120	17.42	0.033	17.51	0.033
150	16.63	0.027	16.66	0.024
180	15.83	0.023	16.03	0.023
210	15.32	0.020	15.26	0.020
240	14.66	0.018	14.88	0.018
270	14.24	0.016	14.32	0.017
300	13.59	0.015	13.77	0.015
330	13.41	0.011	13.47	0.013
360	13.24	0.013	12.97	0.013
390	12.70	0.010	12.63	0.010
405	12.50	0.008	12.40	0.008

[a] Moisture content was calculated on the basis of dry weight of lactose

[b] Operating conditons were: Tunnel temperature, 54°C ± 1°; Air velocity, 11.2 ft/sec; Relative humidity, 40%

Table XVI (cont.)

Moisture Content[a] and Drying Rate in Beds of Lactose[b]

Time (Min)	Run III		Run IV	
	Percent Moisture	Drying Rate (g/min)	Percent Moisture	Drying Rate (g/min)
7.5	23.20	0.076	22.88	0.063
15	22.15	0.068	22.35	0.058
30	21.44	0.053	21.71	0.056
45	20.70	0.057	20.84	0.050
60	19.83	0.050	20.03	0.046
90	18.59	0.043	18.82	0.039
120	17.50	0.030	17.42	0.032
150	16.66	0.024	16.77	0.026
180	16.03	0.023	16.19	0.025
210	15.26	0.023	15.41	0.022
240	14.80	0.016	14.74	0.020
270	14.30	0.018	14.26	0.020
300	13.75	0.015	14.13	0.016
330	13.41	0.015	13.42	0.014
360	12.98	0.012	12.96	0.013
390	12.65	0.006	12.60	0.007
405	12.42	0.007	12.40	0.005

[a] Moisture content was calculated on the basis of dry weight of lactose

[b] Operating conditions were: Tunnel temperature, 54°C ± 1°; Air velocity, 11.2 ft/sec; Relative humidity, 40%

Table XVII

Drying Rate of Lactose[a]

Time (Min)	Drying Rate (g/min) Mean[b]	Range
7.5	0.078	0.023
15	0.069	0.023
30	0.056	0.006
45	0.051	0.013
60	0.046	0.007
90	0.039	0.007
120	0.032	0.003
150	0.025	0.003
180	0.023	0.002
210	0.021	0.002
240	0.018	0.004
270	0.017	0.004
300	0.015	0.001
330	0.013	0.004
360	0.013	0.001
390	0.008	0.004
405	0.007	0.003

[a] Operating conditions were:
Tunnel temperature, 54°C ± 1°;
Air velocity, 11.2 ft/sec;
Relative humidity, 40%

[b] Mean of four runs

Table XVIII

Drying Rate of Lactose - Values Obtained Using Method of Least Squares[a]

Time (Min)	Drying Rate (g/min) Mean[b]	Range
0	0.074	0.022
15	0.068	0.017
30	0.062	0.012
45	0.055	0.015
60	0.048	0.002
75	0.042	0.008
90	0.039	0.007
105	0.036	0.001
120	0.033	0.002
135	0.030	0.006
150	0.025	0.007
165	0.023	0.004
180	0.022	0.003
195	0.021	0.005
210	0.023	0.005
225	0.019	0.006
240	0.014	0.004
255	0.014	0.003
270	0.015	0.007
285	0.016	0.004
300	0.015	0.001
315	0.014	0.005
330	0.013	0.008
345	0.013	0.002
360	0.014	0.001
390	0.013	0.001

[a] Operating conditions were:
Tunnel temperature, 54°C ± 1°;
Air velocity, 11.2 ft/sec;
Relative humidity, 40%

[b] Mean of four runs

Table XIX

Moisture Content Versus Time
in Beds of Calcium Sulfate Dihydrate[a]

Time (Min)	% Moisture Content on Dry Basis		
	Run I	Run II	Mean
0	46.24	45.50	45.87
7.5	45.40	44.20	44.80
15	44.31	43.97	44.14
30	42.14	42.07	42.11
45	40.33	39.83	40.08
60	38.16	37.97	38.06
75	37.10	36.73	36.92
90	36.07	35.56	35.82
105	35.06	34.39	34.73
120	34.34	33.34	33.84
135	33.43	32.81	33.12
150	32.88	32.30	32.59
165	32.26	31.72	31.99
180	31.82	30.99	31.41
195	31.42	30.28	30.85
210	31.10	29.81	30.46
225	30.51	29.50	30.04
240	30.14	29.08	29.61
255	29.75	29.98	29.37
270	29.45	28.72	29.09
285	29.15	28.61	28.88
300	28.88	28.25	28.57
315	28.62	28.20	28.41
330	28.24	28.00	28.12
345	27.98	27.85	27.92
360	27.80	27.60	27.70
375	27.55	27.40	27.48
390	27.28	27.30	27.29
405	27.00	27.00	27.00
420	26.80	26.90	26.85

[a] Operating conditions were:
Tunnel temperature, 54°C ± 1°;
Air velocity, 11.2 ft/sec;
Relative humidity, 40%

Table XX

Drying Rate in Beds of Calcium Sulfate Dihydrate[a]

Time (Min)	Drying Rate (g/min) Mean[b]	Range
7.5	0.126	0.013
15	0.136	0.001
30	0.129	0.005
45	0.121	0.013
60	0.103	0.008
75	0.075	0.002
90	0.061	0.015
120	0.049	0.008
150	0.040	0.000
180	0.035	0.001
210	0.029	0.001
240	0.027	0.001
270	0.018	0.005
300	0.014	0.008
330	0.016	0.009
360	0.015	0.001
390	0.014	0.001

[a] Operating conditions were: Tunnel temperature, 54°C ± 1°; Air velocity, 11.2 ft/sec; Relative humidity, 40%

[b] Mean of two determinations

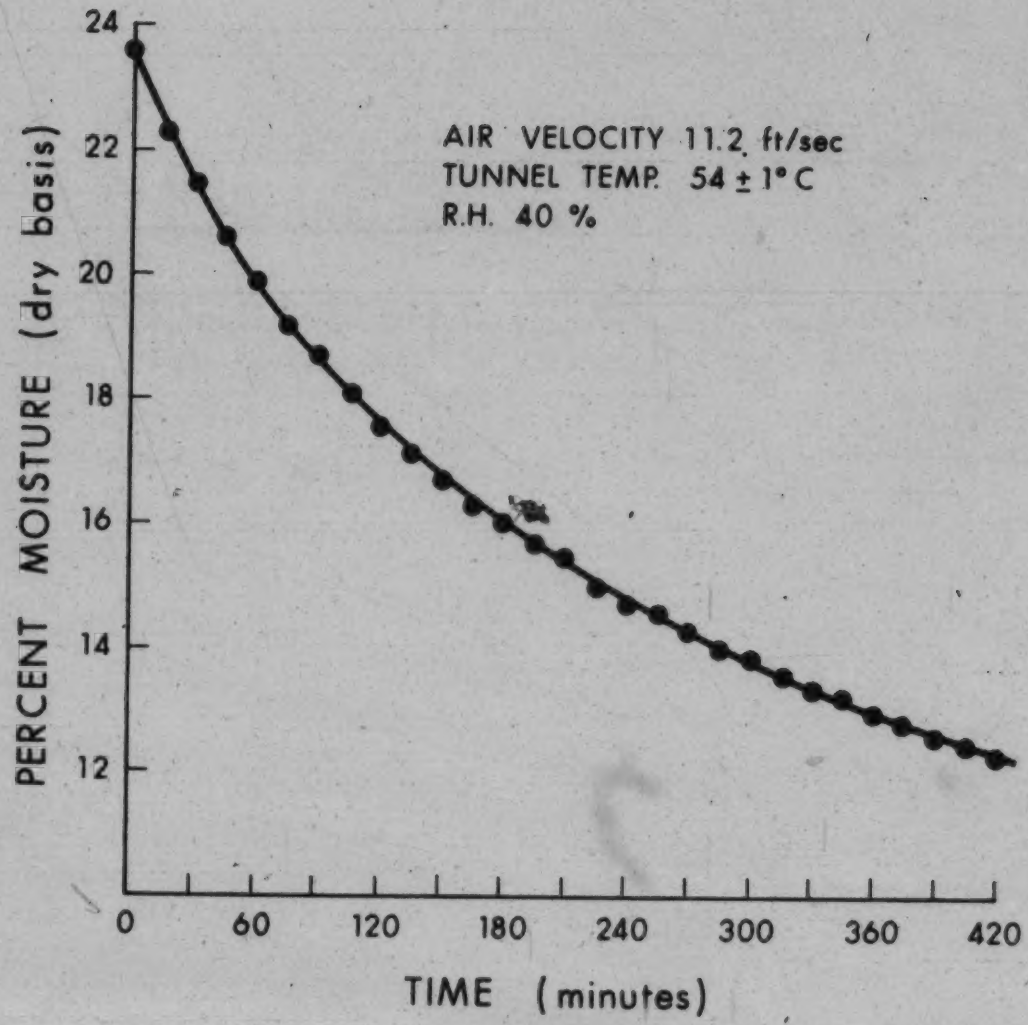

Figure 13

Percent Moisture Content (Mean of Four Determinations) Versus Time in a Lactose Bed

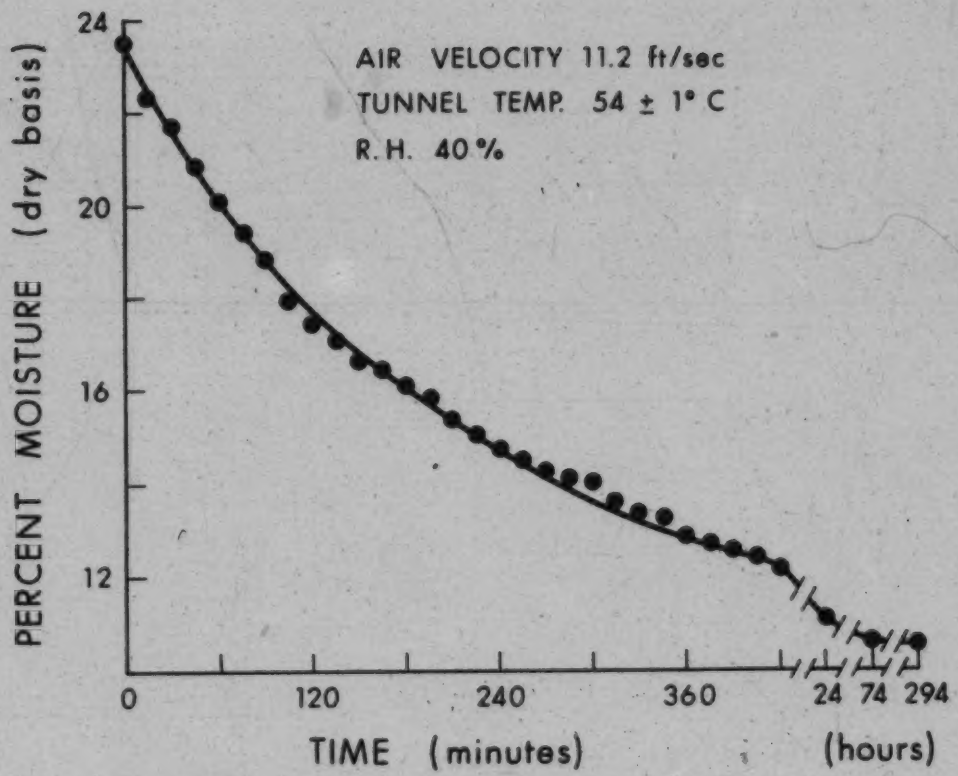

Figure 14

Percent Moisture Content Versus Time
in a Lactose Bed

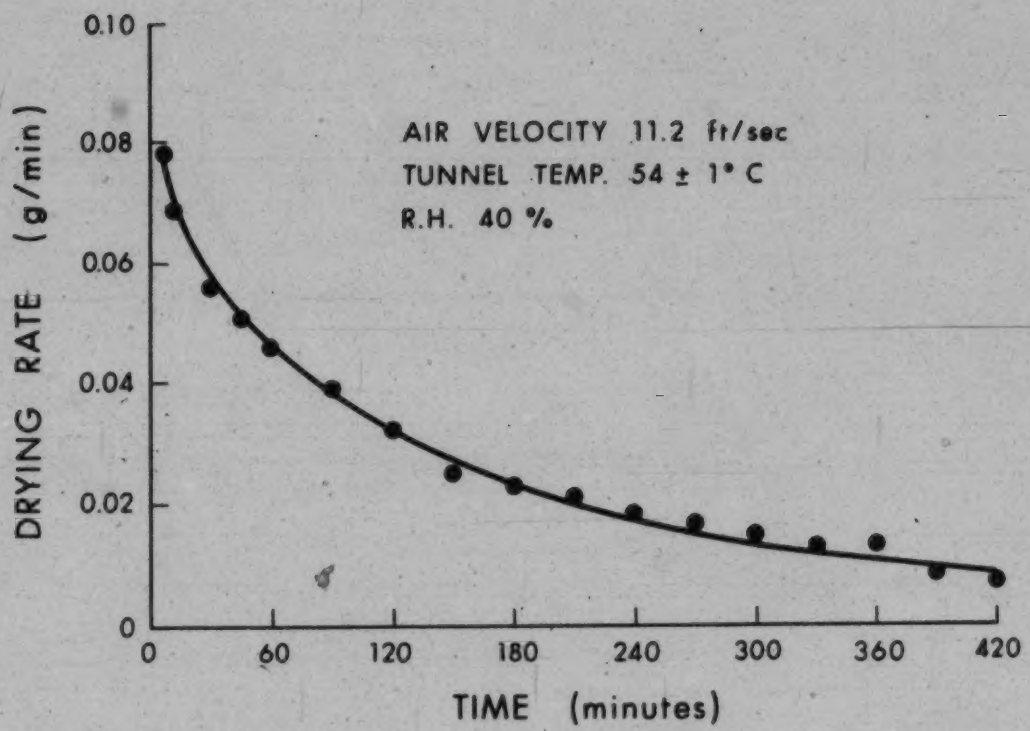

Figure 15

Drying Rate (Mean of Four Determinations)
Versus Time in a Lactose Bed

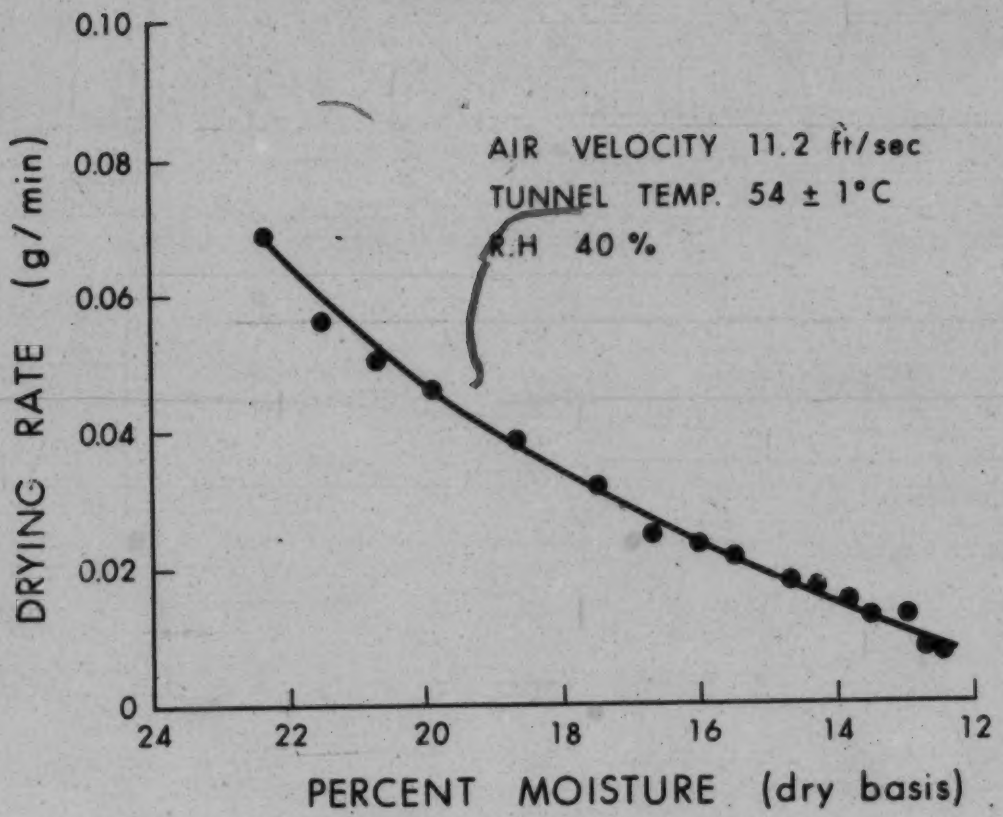

Figure 16

Drying Rate Versus Moisture Content
(Means of Four Determinations)
in a Lactose Bed

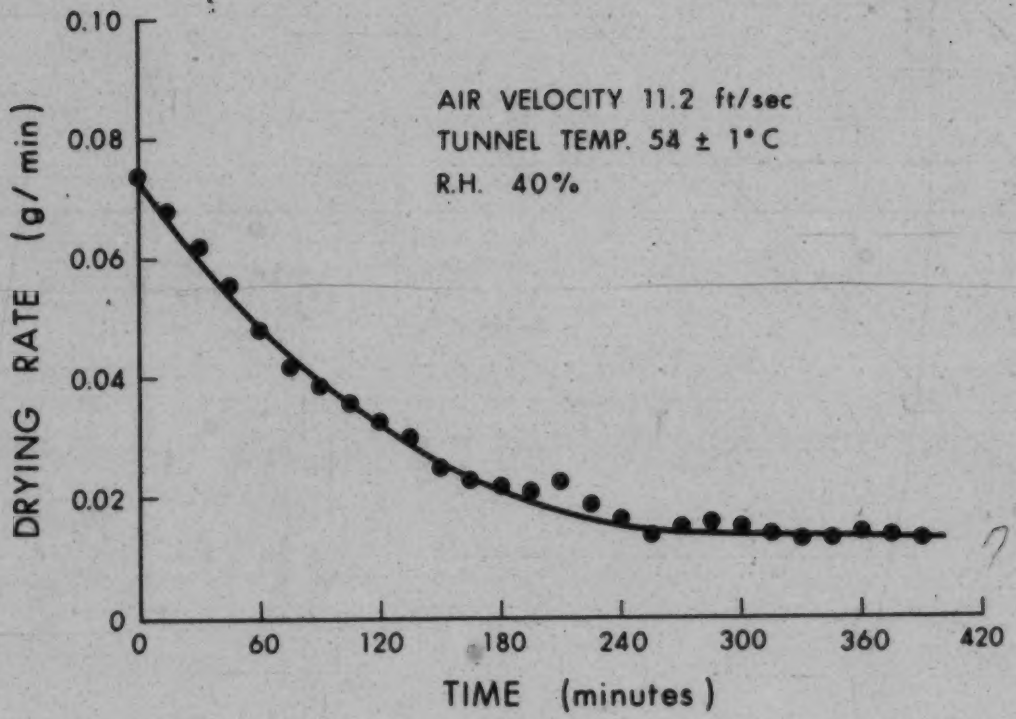

Figure 17

Drying Rate Versus Time in a Lactose Bed
Using the Least Squares Method

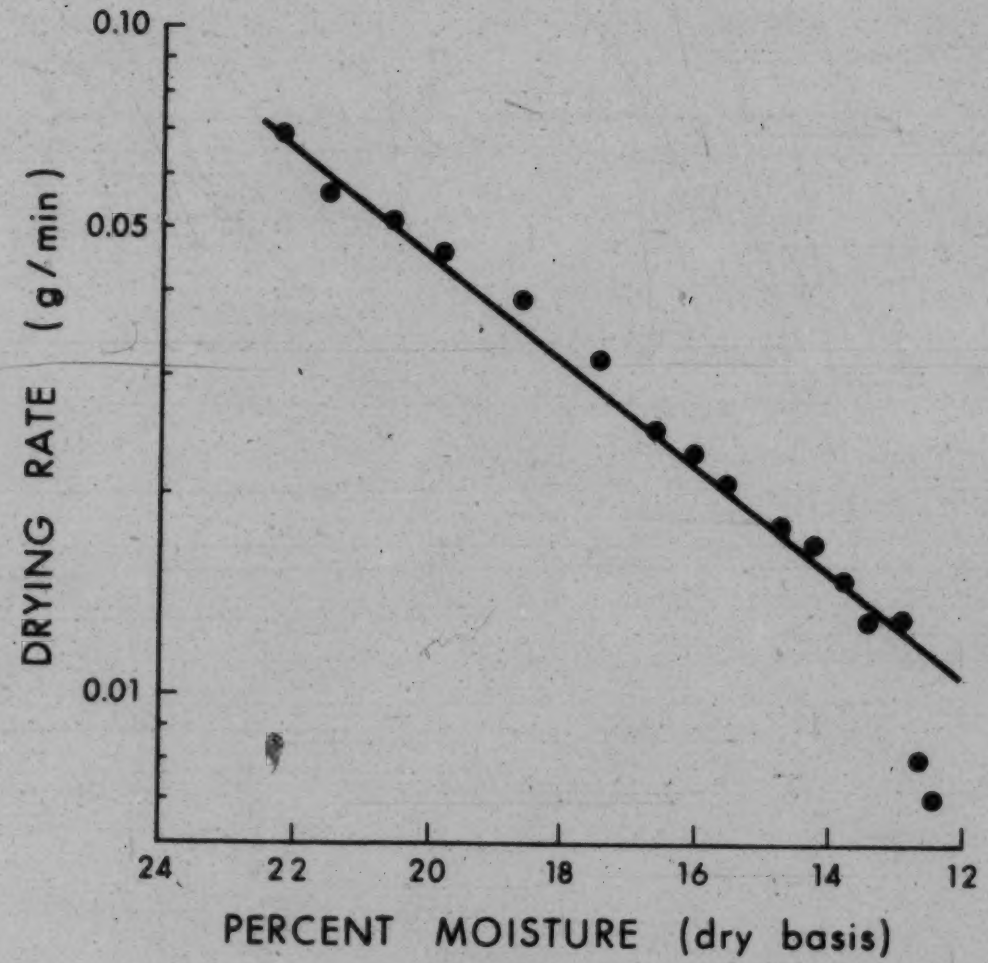

Figure 18

Log Drying Rate Versus Moisture Content
in a Lactose Bed

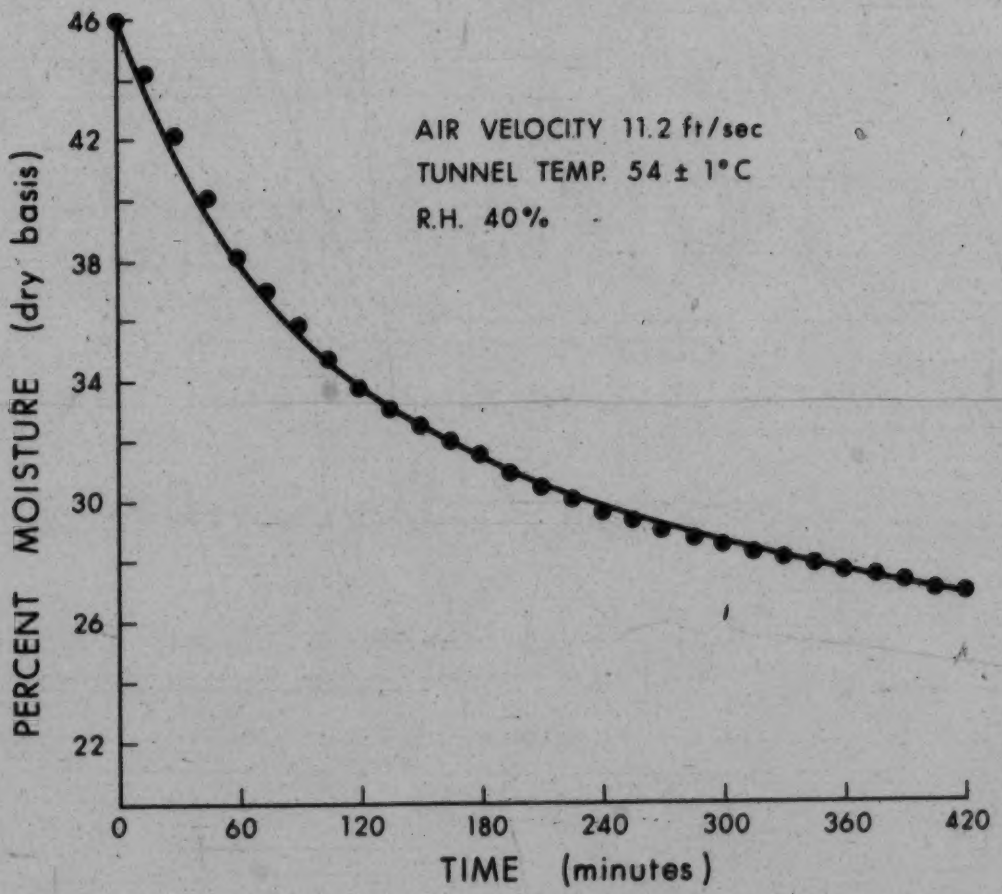

Figure 19

Percent Moisture Content (Mean of Two Determinations) Versus Time in a Calcium Sulfate Dihydrate Bed

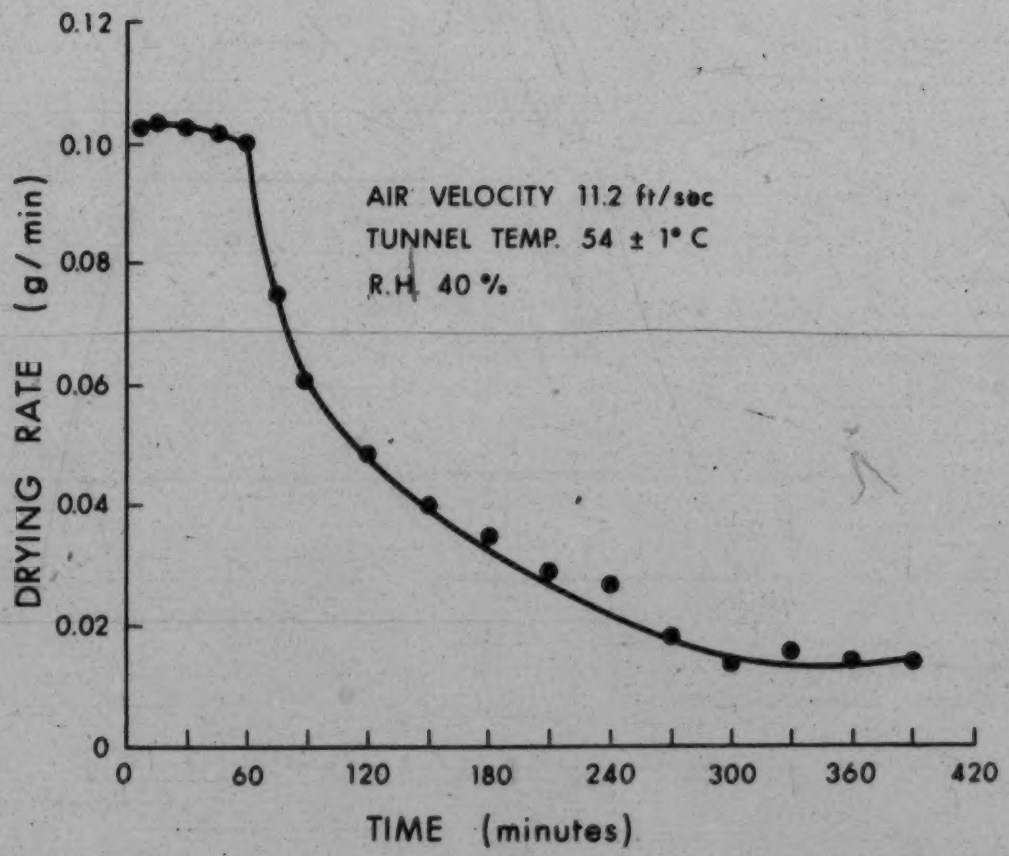

Figure 20

Drying Rate (Mean of Two Determinations)
Versus Time in a Calcium Sulfate Dihydrate Bed

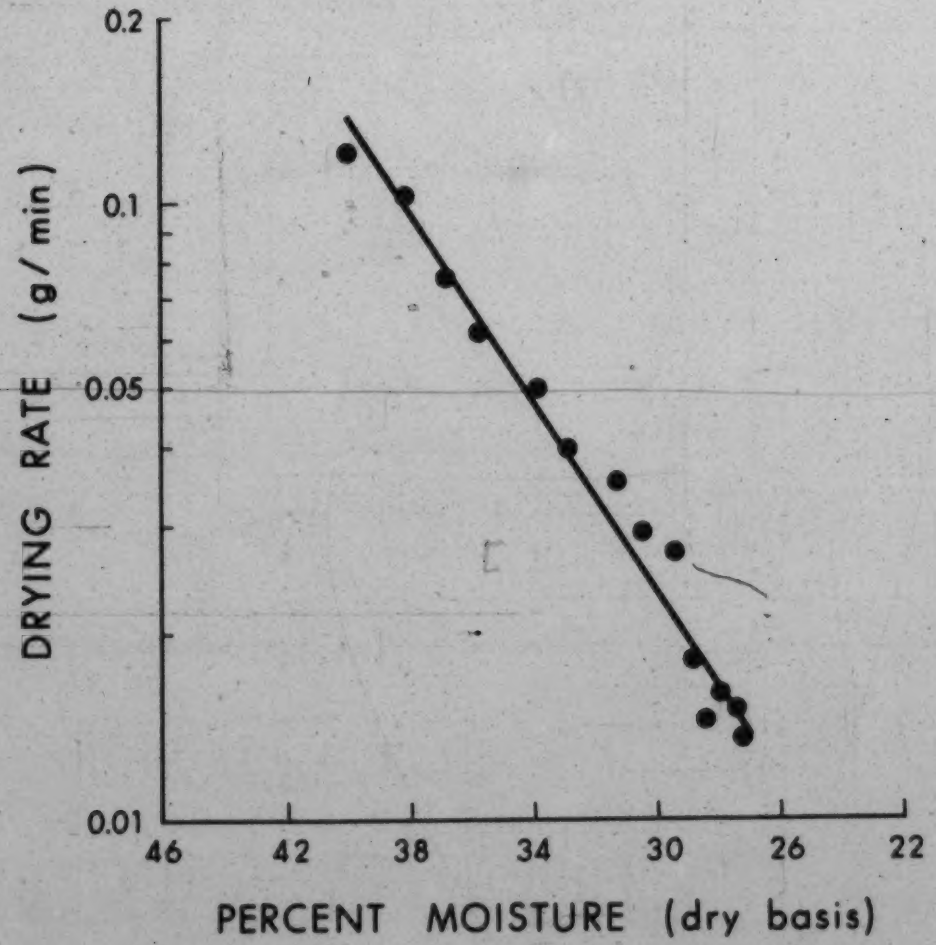

Figure 21

Log Drying Rate Versus Moisture Content
in a Calcium Sulfate Dihydrate Bed

in the moisture content between any two measurements divided by the time period involved. This value was plotted against the mid-point of the time period for a drying rate versus time curve.

This method of obtaining the drying rate curve has been used previously by Bartlett (6). However, Bartlett employed a technique requiring removal of the bed from the tunnel at three-minute intervals for weighing purposes. The weight difference was then divided by the time difference to obtain a very smooth drying rate curve.

Another method used in the calculation of the drying rate is by using the smoothing technique which involves the approximation of the tabulated data by a least-square fit of the data using a second degree polynomial expression.

This method was used for the calculation of the drying rate of lactose. The results calculated by this latter method are shown in Table XIX, and the curve plotted from these data is represented in Figure 17.

Plotting the logarithm of the drying rate versus liquid content for both systems, lactose and calcium sulfate dihydrate, gave a linear plot once the constant rate period had elapsed, as shown in Figure 18 and Figure 21. This was noticed for the first time by Ridgway and Callow in 1967 (21).

9. Solute Migration

A. Calibration Curve for Amaranth Solution

The results of the absorbance of a series of ten amaranth solutions of increasing concentration measured at 522.5 nm using 1 cm cell are reported in Table XXI. The plot of absorbance against concentration gave a rectilinear curve over the range of 0.18 mg to 1.8 mg of amaranth per ml of solution, as shown in Figure 22. This indicates that Beer's law relationship is obeyed over this concentration range.

The slope of the curve was found to be 3.783. This value was used to determine the concentration of the dye in different levels of the bed during migration due to the drying process.

B. Determination of the Effect of the Presence of Lactose on the Absorbance of Amaranth

A "T" test was applied to the data to determine whether the difference between two means is significant (mean absorbance of 0.0013% solution of amaranth in distilled water and in a 1% solution of lactose). The data presented in Table XXII were treated as unpaired data, and the difference was found to be insignificant.

C. Stability of Amaranth Solution

The results for the determination of the stability of amaranth are shown in Table XXIII. From these results

Table XXI

Relationship of Concentration of Amaranth to Absorbance at 522.5 nm

Concentration (mg/ml)	Absorbance		
	Run I	Run II	Mean
0.18	0.076	0.074	0.075
0.36	0.143	0.141	0.142
0.54	0.216	0.216	0.216
0.72	0.278	0.276	0.277
0.90	0.351	0.349	0.350
1.08	0.424	0.247	0.426
1.26	0.483	0.481	0.482
1.44	0.551	0.551	0.551
1.62	0.615	0.625	0.620
1.80	0.678	0.676	0.677

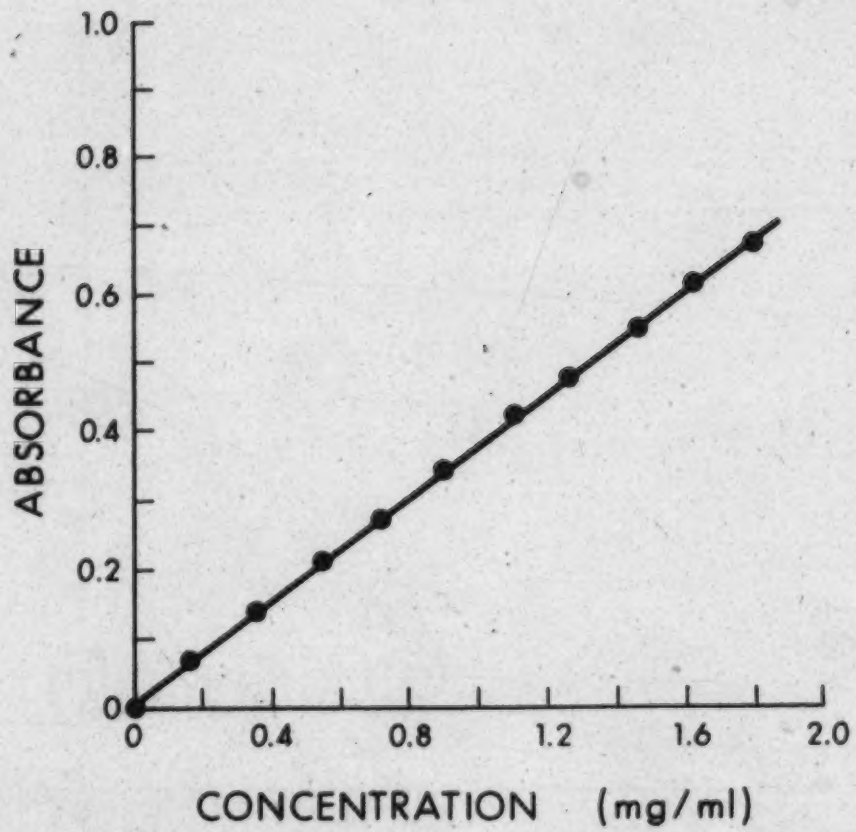

Figure 22

Calibration Curve for Amaranth in Solution

Table XXII

Absorbance of Amaranth in Distilled Water and in a 1% Solution of Lactose

Absorbance of Amaranth in Distilled Water			Absorbance of Amaranth in 1% Lactose Solution		
Run I	Run II	Mean	Run I	Run II	Mean
0.494	0.490	0.492	0.492	0.492	0.492
0.487	0.487	0.487	0.485	0.489	0.487
0.479	0.481	0.480	0.480	0.482	0.481
0.487	0.487	0.487	0.492	0.488	0.490
0.485	0.485	0.485	0.490	0.492	0.491
0.486	0.487	0.487	0.480	0.484	0.485

Table XXIII

Concentration of Amaranth Solution in Percent

	Amaranth Solution	Concentration of Amaranth		
		Run I	Run II	Mean
1.	Unheated solution	0.0442	0.0442	0.0442
2.	Heated solution[a]	0.0438	0.0442	0.0440
3.	Lactose + Amaranth solution[b]	0.0440	0.0440	0.0440
4.	Calcium Sulfate Dihydrate + Amaranth solution[c]	0.0370	0.0376	0.0373

a,b,c These preparations were heated at 55°C for 66 hours

it was concluded that there was no effect on amaranth solution concentration due to heating or due to the presence of lactose. But there was a little significant decrease in the amaranth solution concentration in the presence of calcium sulfate. This could be due to the adsorption of amaranth on the calcium sulfate dihydrate

D. Solute Migration

The results of the determination of migration of amaranth and moisture distribution in beds of lactose and calcium sulfate are shown in Tables XXIV and XXV. The mean value of three determinations of amaranth migration in lactose and calcium sulfate was plotted in Figures 23 and 24. The results plotted in both figures represent the average concentration of amaranth and moisture at the different depths.

These results indicated that amaranth dye migrated with the solvent to the surface of the bed mostly within the first hour of the drying period. After that there was little migration in both systems.

It was noted that most of the dye was deposited in the top layer of the bed to a depth of 0.159 cm. At depths more than 0.317 cm from the surface the beds had a dye concentration less than that of the initial distribution.

The curves of moisture distribution showed that the variation of the moisture content within the beds seems similar, except after about one hour, when the calcium

sulfate bed seems to have dried to a greater depth than the lactose bed.

E. Determination of the Migration of Amaranth in damp Beds of Lactose and Calcium Sulfate

Tables XXIV and XXV show the extent of migration of amaranth and moisture distribution at different depths in beds of lactose and calcium sulfate after drying the beds for different lengths of time.

Table XXIV

Concentration of Amaranth and Moisture Distribution Versus Time in Damp Beds of Lactose

Run No.	Time (Hr)	Distance From Surface (%)	Moisture Content[a] (%)	Concentration of Amaranth[b] (%)
1	0	7.14	14.000	0.028
		14.28	14.608	0.024
		28.57	14.890	0.024
		57.14	14.870	0.024
		87.71	14.860	0.027
		100.00	14.990	0.028
2	1	7.14	6.650	0.084
		14.28	10.475	0.025
		28.57	11.822	0.020
		57.14	11.998	0.020
		87.71	11.774	0.018
		100.00	11.885	0.018
3	2	7.14	3.980	0.088
		14.28	8.360	0.024
		28.57	10.750	0.018
		57.14	9.900	0.017
		85.71	10.800	0.018
		100.00	10.900	0.018

...continued

Table XXIV (cont.)

Run No.	Time (Hr)	Distance From Surface (%)	Moisture Content[a] (%)	Concentration of Amaranth[b] (%)
4	4	7.14	3.380	0.098
		14.28	8.101	0.024
		28.57	8.717	0.017
		57.14	9.915	0.018
		85.71	9.950	0.018
		100.00	9.950	0.016
5	16	7.14	1.614	0.098
		14.28	1.718	0.038
		28.57	2.869	0.012
		57.14	3.440	0.010
		85.71	3.950	0.009
		100.00	3.950	0.010
6	24	7.14	0.714	0.105
		14.28	1.860	0.030
		28.57	2.600	0.007
		57.14	2.742	0.007
		85.71	3.572	0.006
		100.00	4.208	0.007

a,b Mean of three determinations.

Table XXV

Concentration of Amaranth and Moisture Distribution Versus Time in Damp Beds of Calcium Sulfate

Run No.	Time (Hr)	Distance From Surface (%)	Moisture Content[a] (%)	Concentration of Amaranth[b] (%)
1	0	7.14	14.582	0.021
		14.28	14.704	0.021
		28.57	14.890	0.020
		57.14	14.116	0.020
		85.70	15.590	0.017
		100.00	15.660	0.019
2	1	7.14	6.954	0.053
		14.28	8.371	0.025
		28.57	11.385	0.019
		57.14	11.836	0.018
		85.70	11.900	0.018
		100.00	11.998	0.019
3	2	7.14	4.250	0.054
		14.28	8.000	0.025
		28.57	9.980	0.018
		57.14	10.570	0.018
		85.70	10.980	0.017
		100.00	11.000	0.018

...continued

Table XXV (cont.)

Run No.	Time (Hr)	Distance From Surface (%)	Moisture Content[a] (%)	Concentration of Amaranth[b] (%)
4	4	7.14	3.400	0.058
		14.28	7.998	0.028
		28.57	8.780	0.020
		57.14	9.900	0.015
		85.70	9.721	0.015
		100.00	9.951	0.021
5	16	7.14	1.800	0.058
		14.28	1.950	0.027
		28.57	2.790	0.018
		57.14	3.090	0.017
		85.70	3.900	0.018
		100.00	3.980	0.017
6	24	7.14	0.815	0.058
		14.28	1.670	0.031
		28.57	2.000	0.022
		57.14	3.000	0.015
		85.70	3.860	0.015
		100.00	4.000	0.015

[a,b] Mean of three determinations.

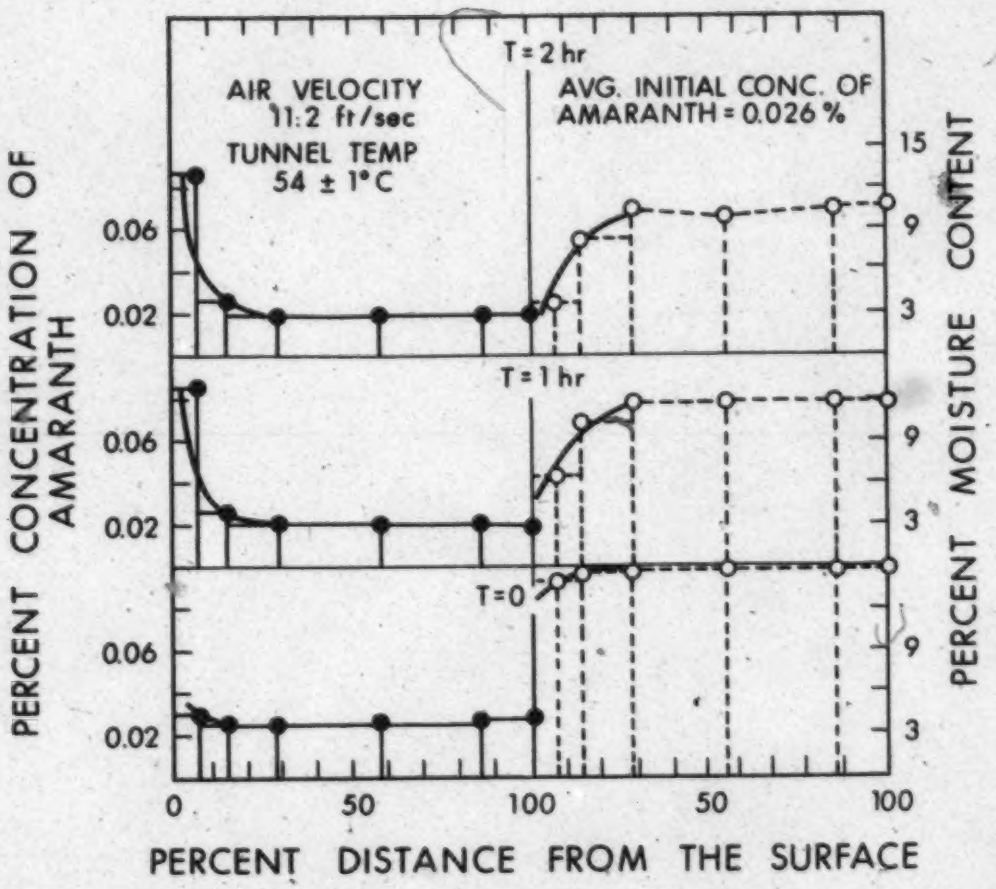

Figure 23

Solute Migration and Moisture Distribution
in Damp Beds of Lactose

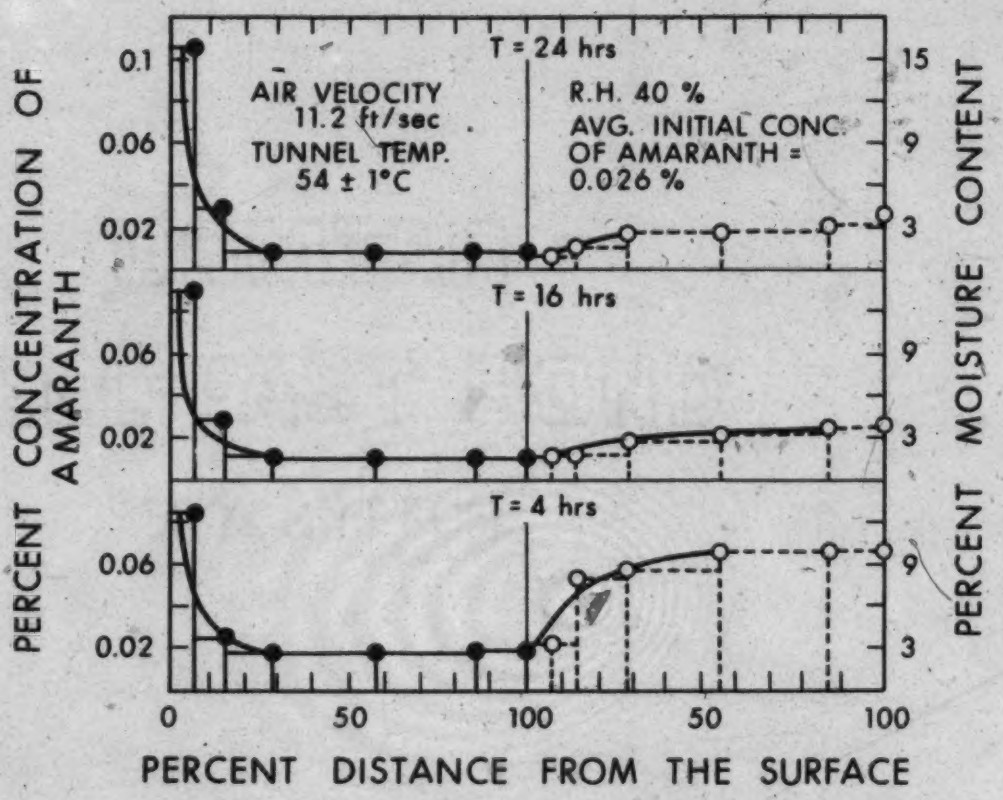

Figure 23 (Continued)

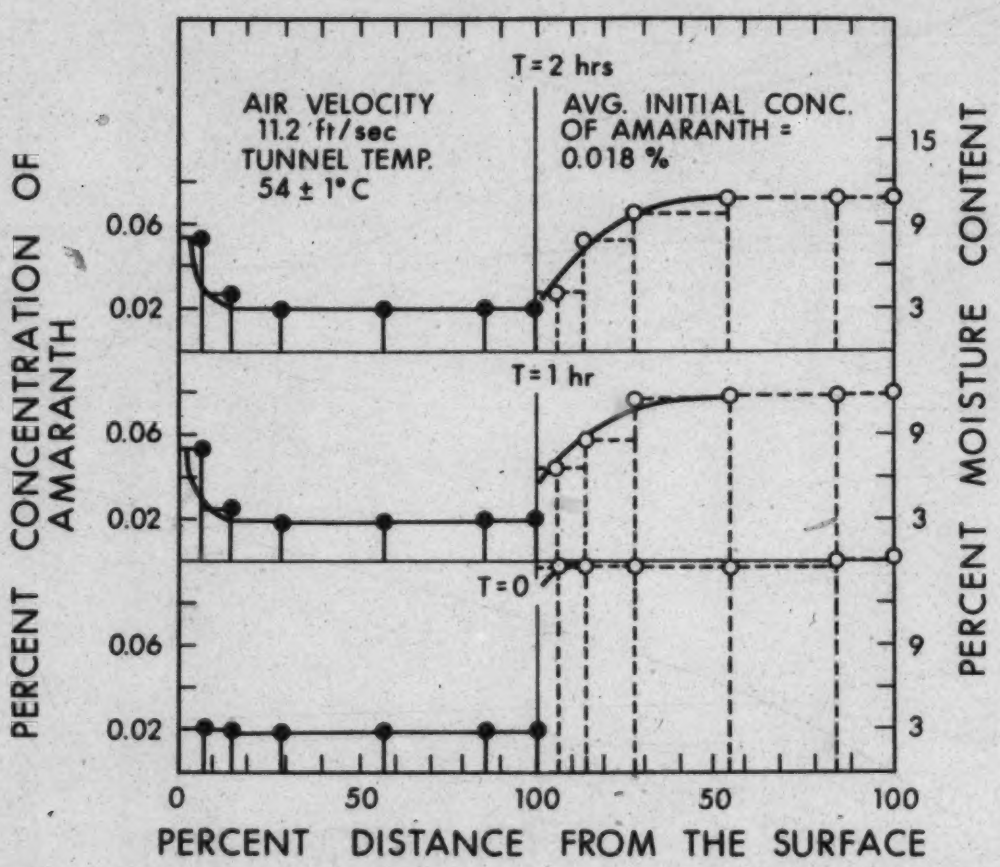

Figure 24

Solute Migration and Moisture Distribution
in Damp Beds of Calcium Sulfate Dihydrate

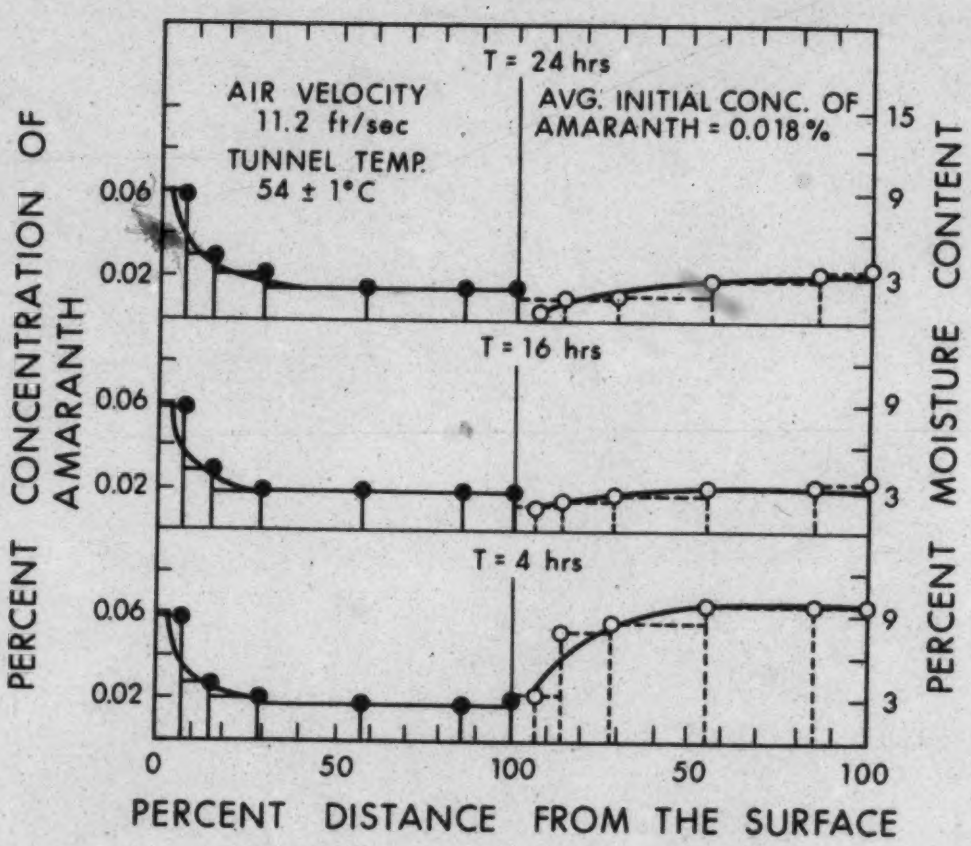

Figure 24 (Continued)

DISCUSSION

1. Calibration of Thermocouples

In designing the project, emphasis was placed on the use of thermocouples to record the temperatures throughout the sample beds. As such, it was essential that accuracy of the thermocouples be verified. The emf values obtained from the calibration procedure were compared with the published data (38). No significant differences between the observed and the literature values were found for the thermocouples used in the present investigation. In fact, a straight line relationship was found when the emf values were plotted as a function of temperature. Calibration of the thermocouples was repeated a number of times during the study. No significant differences were obtained among the observed values, indicating a sensitive and highly reproducible recording system.

2. Effect of Conduction of Heat Along the Wire to the Junction

Statistical analysis of the data presented in Tables IV and V showed that the heat conducted along the wire to the junction was insignificant. On the basis of these results it was concluded that any error involved in the powder bed temperature recordings could be ignored.

3. Determination of Mean Air Velocity Through the Tunnel at Room Temperature

From the results shown in Table VI, it may be seen that the use of the shaped baffle plate inserted between the fan and the tunnel produced a satisfactory air distribution through the cross-sectional area. It was found that the fan had to be left in operation for at least 30 minutes in order to stabilize air flow at the required velocity before starting the experiment. As a precautionary measure the air velocity determination was repeated at regular intervals to ensure reproducibility of the results.

4. Temperature Distribution

The results obtained for the temperature distribution in beds of lactose using different containers are shown in Figures 7, 8 and 9. A close study of these figures showed that further insulation of the bed with the glass wool had no significant effect on temperature distribution. For this reason it was felt that containers coated with epoxy resin alone would be satisfactory.

The results obtained in beds of lactose and calcium sulfate showed that the temperature near the wall was consistently higher than that at the center of the bed at the same level. To account for this relationship, it was assumed that the surface of the bed acted as an excellent insulator while vaporization was occurring there, since most of the heat received from the air stream was used to

vaporize the water, which was then carried away by the air stream.

Adams (7) suggested that the void fraction was greater near the smooth walls of the box. Therefore most of the air entering the lower depths of the bed probably flowed down the walls rather than through the center of the bed where the voids were slightly smaller. Adams postulated that this air became saturated near the surface of the bed and then passed down into the cooler depths causing condensation and release of the heat of vaporization in the bed near the walls.

This concept did not seem to fully explain the results obtained in this study, probably because of the nature of the bed. The particles and voids involved are much smaller than those in Adams' work. Since the bed was a damp mass, it was thought that a thin layer of moisture may have existed in contact with the smooth inner walls of the cup. It was then assumed that most of the heat entering the lower layers of the bed would have a tendency to flow down the sides rather than through the center of the bed. Other factors were also thought to contribute to the higher temperature at the walls of the containers. One of these factors could be conduction through the wall of the sample container due to imperfect insulation.

The bed material was considered to be composed of solid and void fractions. Heat transfer would then occur

in the bed by conduction in the solid and in the air-filled voids. Convection and radiation may also be operative in the voids. For small temperature differences, however, the effect of radiation would be small, and convection would be important only if the bed possessed a very open structure.

This fact would suggest that heat transfer through the bed occurred mainly by conduction. The powder bed started at almost a uniform temperature, and when it was subjected to the warm air flowing over the surface, a temperature gradient was set up. The bed surface then reached a higher temperature rapidly but layers at greater depths took longer to adjust.

The surface temperature in the calcium sulfate bed attained the wet-bulb temperature with the heat transferred from the warm air and surroundings being used in evaporating water from the surface. However, as drying continued, the volume of water on the surface became so depleted that the surface no longer behaved as it did when thoroughly wet. In fact, the rate of evaporation decreased, and of course the rate of heat consumption was likewise decreased. This situation required a decrease in the temperature difference, since the heat transfer coefficient and heat transfer area were the same. With constant air temperature this necessitated a rise in temperature at the surface. These results are in agreement with similar measurements reported by Nissan *et al.* (18,19,20), and Adams (7).

The temperature in different depths of the bed after the first falling rate period did not approach a uniform value (pseudo-wet-bulb temperature). This result disagreed with the findings of Nissan et al. (18) and Adams (7). Similarly, Park (40), in his work to establish the pseudo-wet-bulb temperature in different materials, claimed that the effect of this temperature in most of the systems examined was not as marked as in the work of Nissan et al. (18,19,20). However, it was thought that the moisture content in the system studied in the present investigation does not fall off as sharply as in the experiments treated by Nissan. As a result, vaporization would occur over a thicker region of the material.

From the results of the temperature distribution study it was found that the surface temperature in lactose beds did not attain the wet-bulb temperature. This was thought to be due to the low initial moisture present in the bed. It was also found that a pseudo-wet-bulb temperature did not become established through the bed. From the above results it was concluded that conditions needed to establish a pseudo-wet-bulb temperature in the bed were not achieved.

5. Observation of Bed Surface After Drying

After completion of drying runs using lactose and calcium sulfate, it was found that a crust had developed

on the lactose surface but not on the calcium sulfate surface. It was thought that the solubility of lactose in water promoted the crust formation on the surface. This will be discussed further under the heading "Drying Rate".

6. Determination of the Permeability of the Bed Container to Water Vapor

From Table VII it may be seen that the bed container used in the experiment was permeable to water vapor. Since the experiment in the present investigation was designed to expose only the upper surface of the bed for evaporation, it was thought that the use of epoxy resin might help to overcome this problem. As is evident from the results presented in Table VII, the use of epoxy resin coating for the polystyrene cups used was successful in rendering them impermeable to water vapor.

7. Drying Rate

From the results presented in Tables XV - XXII and Figures 12 - 24, it is seen that the drying cycle can be divided into two distinct zones, constant rate period and falling rate period. In the constant rate period, drying takes place from the exposed surface of the bed. In general, the rate of surface evaporation is determined by the rate of diffusion of water vapor through the stationary layer of air in contact with the bed. This diffusion is

proportional to the difference between the partial pressure of the water on the surface of the bed and that in the drying air. However, the rate of diffusion will increase with increased air velocity due to decreasing thickness of the air layer. The falling rate period is considered to be divisible into two secondary periods or zones, which may be termed the zone of unsaturated surface drying and the zone of internal liquid flow. The former follows immediately after the critical point; the decrease in the rate of drying in this zone is due to a decrease in the area of the wetted surface of the material. The surface is no longer completely wetted, and the rate of evaporation per unit of total surface is thereby reduced. The mechanism of drying in this phase is essentially the same as drying in the constant rate period, so that the rate is apparently independent of the thickness of the material being dried.

During the zone of unsaturated surface drying, water diffuses to the surface as fast as it is evaporated and it may be said that the resistance to internal liquid diffusion is small compared with the resistance to diffusion of vapor through the surface air film. The maximum rate of diffusion of water to the surface, however, decreases with the decrease in the water content of the material, so that a second critical point is reached beyond which the resistance to the internal liquid diffusion is greater than the surface resistance to the vapor removal.

During the second zone of the falling rate period, the rate of internal vapor diffusion and the rate of heat conduction controls the rate of drying. The drying rate curve of lactose and calcium sulfate in the falling rate period shows no evidence of a second critical point, as the points fall on a smooth curve of gradually decreasing slope. This shape of the drying rate curve is obtained when internal liquid diffusion controls the rate of drying (14). The results obtained therefore suggest that internal diffusion of the moisture through the solid was a controlling factor during the later stages of drying for both the lactose and calcium sulfate systems. However, it was thought that in the first part of the falling rate period in the lactose drying rate curve (Figure 15), evaporation was primarily a surface phenomenon. This concept was supported by the results presented in Table XXIII on solute migration in beds of lactose. It also agreed with the results obtained by Ridgway and Callow (21). The lactose drying rate curve did not show a constant rate period. This was attributed to the low initial moisture content of the bed. It was found that the rate of drying of calcium sulfate dropped by almost 50% at the end of the constant rate period. The formation of a crust on the surface of lactose early in the drying process was at first thought to produce a delay in the drying of the system, but results failed to support this idea. Data presented in Table XVI

and Figure 14 record the drying of a lactose bed over a period of 294 hours. These results showed that the amount of moisture present in the bed was equal to its equilibrium moisture content (EMC). This was consistent with the fact that anhydrous air was not used to dry the beds. It has been suggested that some of the nonporous solids generally show relatively low EMC over a wide range of relative humidities. For example, Scott, Liberman and Chow (39) showed that the final moisture content of a placebo granulation consisting of 85% lactose, after wet granulation with water, was not affected by a decrease from 70% to 30% in the relative humidity of the drying air. Using the method of least squares for calculating the drying rate of lactose as shown in Table XIX did not improve the drying rate curve, particularly in the final stages of the drying process when the drying rate was fairly low.

Examination of Figures 23 and 24 showed that at one hour drying time the calcium sulfate bed seemed to have dried to greater depths compared with the lactose bed. This could also be due to the difference in particle size as well as difference in void fraction in the two beds. It was believed that the voids in the calcium sulfate beds were larger than the voids in the lactose beds.

Plotting the logarithm of the drying rate against liquid content gave a linear plot once the constant rate period had elapsed. This has been noticed in both systems,

lactose and calcium sulfate (Figures 18 and 21). A similar finding was obtained by Ridgway and Callow in 1967 (21).

It was found from the data for moisture distribution as presented in Figures 23 and 24, that evaporation *in situ* was the operative mechanism in the systems involved in this study. This mechanism is different from that operating in the system studied by Ridgway and Callow. Their mathematical analysis for this relationship seemed to agree with the mechanism operating in the system they examined. However, their theoretical treatment was not confirmed experimentally. Further, they did not mention in their study that this relationship would not hold if the drying mechanism were different from the one operating in their system.

8. Calibration Curve for Amaranth Solution

In terms of absorbance, a linear relationship was found to exist over the concentration range of 0.18-1.80 mg of amaranth per ml. Repeated testing during the course of the experimental work confirmed the stability of the amaranth color.

9. Stability and the Effect of the Presence of Lactose and Calcium Sulfate on the Absorbance of Amaranth

From Table XXIII it was found that the heating and the presence of lactose with amaranth did not interfere with the measurement of the concentration of the dye. On the other hand, the presence of calcium sulfate in

combination with amaranth resulted in a decrease in the initial concentration of the amaranth solution used. It was thought that since amaranth is a water-soluble dye, the decrease in its concentration was probably due to its adsorption on calcium sulfate. In other words, calcium sulfate had an ability to adsorb some of the dye to a measurable extent.

10. Solute Migration

An examination of Figures 23 and 24 shows the migration of amaranth in beds of lactose and calcium sulfate. It is evident that the maximum migration of the dye to the upper layer of the bed took place in the early stages of the drying period. Later there was only a little migration in either system. The continuous increase in the concentration of the dye at the surface of the bed suggested that any back diffusion due to the concentration gradient was small compared with the forward flow of the solution during the drying process. This did not agree with the data for PVP as reported by Ridgway and Rubinstein (27). It was thought that the method of back diffusion depends upon arresting drying at the stage when liquid movement ceases, then sufficient time is allowed for the solute to redistribute itself by diffusion. The drying process is then carried to completion. Quantitative analysis of the concentration of amaranth in beds of lactose and calcium sulfate

showed that the concentration of amaranth at the surface of the calcium sulfate bed was less than that on the surface of a lactose bed. The degree to which color migration occurs in granulations is said to depend on several factors, e.g. the water solubility of the dye, the drying conditions under which the granulation is dried, and the excipients present (41,42). Therefore, since the solubility of the dye and the drying conditions of the experiment were constant, it was concluded that the migration of the amaranth was a function of the system and, in fact, was characteristic of each solid involved. This argument could be supported by the results shown in Table XXIII, which showed the ability of calcium sulfate to adsorb amaranth to a small but measurable extent. This affinity of calcium sulfate or any other substrate toward the dye or a drug substance has been confirmed by Chaudry and King (28), Robert E. King (41) and Jaffe and Lippmann (42).

An approach for explaining the migration of amaranth in both systems (lactose and calcium sulfate) could be reached by reference to liquid and vapor migration during the drying process. First consider what happened in the upper half of the bed. As the moisture content decreased from its initial values corresponding with those of constant and first falling rate periods, liquid moved to the surface and evaporated. As the moisture content further decreased to a point to correspond to that during the second falling

rate period, pendular liquid vaporized *in situ*. As the moisture content decreased further, the moisture movement was insignificant as shown by the moisture distribution as well as the dye measurement at this zone.

From the results presented in Figure 23 a small difference was noticed in amaranth concentration between 16 and 24 hours at the top of the lactose bed. However, this increase was very small and could be attributed to experimental error.

Now consider the lower half of the bed. By the time the critical point was reached, some liquid had already been removed from the base of the bed, probably by capillary movement.

The concentration of the dye present in this zone indicated that initially only a small part of the total vaporization took place here.

The uniform but slow reduction in moisture content and dye concentration in the lower part of the bed during the later stages of drying indicated that some capillary flow of liquid toward the surface was taking place. It was initially thought that evaporation was taking place at a uniform rate in this zone, but this mechanism was rejected because of the differences in temperature (5 - 8°C) between top and bottom of the zone and the consequent differences in driving force for evaporation.

SUMMARY

1. Drying conditions under which the experiments were run were established.

2. Temperature distribution curves were established for both lactose and calcium sulfate. From these measurements it was found that the temperature varied to a greater extent in the calcium sulfate bed than in the lactose bed.

3. Drying rate curves were constructed for both systems after drying the beds under constant drying conditions. No clear distinction between the first and second falling rate periods was observed.

4. A technique was developed for sectioning the powder bed by using a lathe milling machine. The developement of technique helped in the determination of the moisture content and solute migration at different depths of the bed.

5. Moisture distribution through the bed at different depths was determined gravimetrically. These results showed that capillary movement was the operative mechanism in the early stages of drying. It was also found that evaporation of water within the bed was operative in the latter stages of drying. Because of the different mechanisms operating at different depths of

the bed at different times, simple analysis of the drying mechanism was not possible.

6. A sample changer unit integrated with the sp600 spectrophotometer was used for the quantitative analysis of the migrated amaranth through the bed. The results showed that migration occurred in both systems in the early stages of the drying process. It also confirmed the capillary movement at these stages.

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